CHEMISTRY OF STRAINED POLYCYCLIC SYSTEMS

A Thesis Submitted
in partial Fulfilment of the Requirements
for the Degree of
DOCTOR OF PHILOSOPHY

By
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to the

DEPARTMENT OF CHEMISTRY
INDIAN INSTITUTE OF TECHNOLOGY KANPUR
MARCH, 1976

TO

MY PARENTS

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STATEMENT

I hereby declare that the matter embodied in this thesis is the result of investigations carried out by me in the Department of Chemistry, Indian Institute of Technology, Kanpur, India, under the supervision of Professor G. Mehta.

In keeping with the general practice of reporting scientific observations, due acknowledgement has been made wherever the work described is based on the findings of other investigators.

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CERTIFICATE I

This is to certify that Mr. Paras Nath Pandey has satisfactorily completed all the courses required for the Ph.D. degree programme. These courses include:

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Chm 521	Chemical Binding
Chm 523	Chemical Thermodynamics
Chm 541	Advanced Inorganic Chemistry I
Chm 502	Advanced Organic Chemistry II
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Certified that the work "Chemistry of Strained Polycyclic Systems" has been carried out by Mr. Paras Nath Pandey, under my supervision and the same has not been submitted elsewhere for a degree.

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Thesis Supervisor

ACKNOWLEDGEMENTS

I would like to express my deepest gratitude to Prof. G. Mehta for his inspiring and unfailing guidance throughout the course of the present investigation. I can say with firm convinction that without his enthusiasm and support, I would have been handicapped by mere trivialities and the pleasure of research would have eluded me.

All members of the faculty of the Department have been extremely helpful during my stay, and I wish to thank them all, in particular Professors M.V. George and D. Devaprabhakara.

It is a pleasure for me to thank my colleagues in the Department who have been of invaluable help to me. I wish to mention particularly Dr. S.K. Kapoor, who trained me as a chemist and provided a lively atmosphere throughout my stay The ebullient and helpful nature of Messrs B.P. Singh, Bipin Pandey, K.K. Dwivedi and H.S. Mishra made my stay extremely pleasant. I wish to thank Messrs B.G.B. Gupta, B. Chaudhuri, A. Kumar, M.M. Mehrotra, P. Ghosh, S.C. Suri, C.B. Rao and other innumerable friends for their valuable help in one way or the other. My thanks are also due to some of my friends at B.H.U., Varanasi, in particular, Dr. R. Singh, Mr. Bipin and Mr. Prem N. Pandey, for their generous help of all kinds.

I wish to acknowledge the help received from Prof. G.B. Singh (B.H.U., Varanasi), Dr. Nityanand (C.D.R.I., Lucknow),

Dr. T.-L. Ho (University of Manitoba), and Dr. K. Venkatesan (I.I.Sc., Bangalore) for their immense help in obtaining the PMR and Mass Spectra reported in this thesis.

My thanks are due to Mr. A.H. Siddiqui of Microanalysis Lab., Mr. M.D. Pandey and L.P. Tripathi of Chemistry Stores, and members of Glass Blowing Shop for their help and co-operation. A special word of appreciation is due to Mr. R.D. Singh (for typing), Mr. R.K. Bajpai (for tracing) and Mr. B.N. Shukla (for cyclostyling) for their sincere help in the preparation of this thesis.

Financial assistance from the Council of Scientific and Industrial Research, in the form of a Junior Research Fellowship and a Senior Research Fellowship is gratefully acknowledged.

I wish to express my deepest gratitude and respect to my parents, brother and uncle Shri R.S. Upadhyaya for their constant encouragement and for taking keen interest in my education.

I wish to express my heartfelt appreciation to my wife for her immense patience, understanding and forbearence during the past so many years. Lastly, my little daughter had always a complaint against me that she could not get her share of time to play with me; I accept it.

March 1976 Paras Nath Pandey

PREFACE

Interest in the Chemistry of small strained polycyclic molecules is at an all time high. Newer developments in synthetic methodology, in particular the discovery of intramolecular photochemical cycloadditions, orbital symmetry controlled bond reorganisations and transition metal catalysed valence isomerisations have rendered available here-to-fore elusive molecules in quantities sufficient for chemical exploration. These synthetic developments have stimulated keen interest in the study of transformations and rearrangements of strained polycyclic systems. As a consequence, numerous fascinating and mechanistically intriguing transformations of strained systems have been unravelled during the past fifteen years, resulting in better understanding and appreciation of the nature of transition states, factors influencing carbonium ion rearrangements and strain-reactivity relationships. The research described in the present thesis deals with several diverse and interesting aspects of the chemistry of strained polycyclic molecules.

The thesis entitled, "CHEMISTRY OF STRAINED POLYCYCLIC SYSTEMS" is divided into four chapters, 1: Stereochemistry and mechanism of electrophilic additions to tricyclo$[4.2.2.0^{2,5}]$-deca-3,7-diene derivatives, 2: Novel transannular cyclisations of tricyclo$[4.2.2.0^{2,5}]$deca-3,7- diene ring system,

3: A fascinating 1,3-bishomocubane $\rightarrow$brendane rearrangement, 4: Regiospecific Baeyer-Villiger oxidation of polycyclic ketones with ceric ion. The subject matter of each chapter has been organised under the headings: Abstract, Introduction, Results and Discussion, and Experimental. A brief coverage of literature, relevent to the contents of each chapter, has been provided to serve as useful background material.

1. Stereochemistry and mechanism of electrophilic additions to tricyclo $[4.2.2.0^{2,5}]$deca-3,7-diene derivatives

Addition of several electrophiles to three tricyclo-$[4.2.2.0^{2,5}]$deca-3,7-diene derivatives, readily available from cyclooctatetraene-maleic anhydride adduct has been investigated. The stereochemistry of addition as well as the structure of the addition products has been mainly deduced by the application of pmr spectroscopy. Addition of iodine azide and mercuric acetate to tricyclo$[4.2.2.0^{2,5}]$deca-3,7-diene proceeds in a regio- and stereospecific manner. Thus, iodine azide adds exclusively to the cyclobutene double bond to furnish a cis-azido iodide. This represents the first example of cis-addition of iodine azide to an olefin. Similarly, hydroxy- and methoxymercuration of tricyclic diene system results in cis-oxymercuration of the cyclobutene double bond. The exclusive cis-addition of iodine azide and mercuric acetate observed here is interpreted in terms of the dominant role of twist strain theory. On the other hand, benzenesulphenyl chloride known for its propensity for trans-additions, reacts with

tricyclo$[4.2.2.0^{2,5}]$deca-3,7-dienes in a non-stereospecific manner to furnish both cis- and trans-addition products. This result is best rationalised in terms of a carbonium ion intermediate and discounts the involvement of episulphonium ion intermediate in the product determining step.

2. Novel transannular cyclisations of tricyclo$[4.2.2.0^{2,5}]$-deca-3,7-diene ring system

The tricyclo$[4.2.2.0^{2,5}]$deca-3,7-diene system can be formally considered as a bridged 1,5-cyclooctadiene derivative and is therefore amenable to transannular cyclisations. Electrophile induced cyclisations of 9,10-dicarbomethoxytricyclo-$[4.2.2.0^{2,5}]$deca-3,7-diene observed previously by Reppe, Nenitzescu and Cookson have been reinvestigated. It is established that addition of bromine, pyridinium hydrobormide perbromide, iodobenzene dichloride, iodine monochloride and iodine mononitrate to the tricyclic diene proceeds via a novel transannular cross-bonding of the proximal double bonds. These findings, though at variance with the earlier reports, are in analogy with the generally encountered mode of transannular cyclisation of 1,5-cyclooctadienes. The epoxide derived from 9,10-dicarbomethoxytricyclo$[4.2.2.0^{2,5}]$deca-3,7-diene undergoes acid catalysed rearrangement with transannular π-participation. The structure of the resulting tetracyclic alcohol has been established and the mode of cyclisation correlated with that observed with other electrophiles.

3. A fascinating 1,3-bishomocubane → brendane rearrangement

A novel, unanticipated rearrangement of pentacyclo-[5.3.0.$0^{2,5}$.$0^{3,9}$.$0^{4,8}$]-decan-6-one (1,3-bishomocubanone) to a 2,9-disubstituted tricyclo[4.2.1.$0^{3,7}$]non-4-ene (brend-4-ene) derivative has been encountered during Schmidt reaction conditions. Reaction of 1,3-bishomocubanone with sodium azide in methanesulphonic acid medium led to the formation of exo-2-methanesulphonoxy-9-cyanobrend-4-ene in good yield. The structure of the disubstituted brend-4-ene derivative has been established through a facile base catalysed 1,3-elimination to 2-cyanodeltacyclene. On sensitised photolysis, 2-cyanodeltacyclene underwent a smooth $\sigma^2_s + \pi^2_s$ cycloaddition to 2-cyanonorsnoutane. These transformations delineate the carbocyclic ring system present in the product obtained from Schmidt fission of 1,3-bishomocubanone. The formation of brend-4-ene framework from 1,3-bishomocubanone represents an interesting $C_{10} \rightarrow C_9$ rearrangement controlled by favourable thermodynamic changes. A plausible mechanism is advanced to rationalise this rearrangement.

4. Regiospecific Baeyer-Villiger oxidation of polycyclic ketones with ceric ion

Efficient and preparatively useful Baeyer-Villiger (BV) oxidation of a few strained polycyclic ketones with ceric ion has been investigated. Oxidation of pentacyclo-[5.3.0.$0^{2,5}$.$0^{3,9}$.$0^{4,8}$]decan-6-one (1,3-bishomocubanone), pentacyclo[5.3.0.$0^{2,6}$.$0^{3,9}$.$0^{4,8}$]decan-5-one (1,4-bishomocubanone) and pentacyclo[6.2.1.$0^{2,7}$.$0^{4,10}$.$0^{5,9}$]undecan-3,6-

dione with ceric ammonium nitrate (CAN) and ceric ammonium sulphate (CAS) yields the corresponding lactones in high yield. For comparison, peracid oxidation of the three pentacyclic ketones has also been investigated. It has been observed that ceric ion oxidation of unsymmetrical 1,3-bishomocubanone and pentacyclo $[6.2.1.0^{2,7}.0^{4,10}.0^{5,9}]$ undecan-3,6-dione proceeds regiospecifically to yield lactones different from those obtained by conventional peracid oxidation. This observation may be of general synthetic utility in carrying out regiospecific BV oxidation of geometrically constrained polycyclic ketones with ceric ion.

CHAPTER I

STEREOCHEMISTRY AND MECHANISM OF ELECTROPHILIC ADDITIONS TO TRICYCLO[4.2.2.$O^{2,5}$]DECA-3,7-DIENE DERIVATIVES

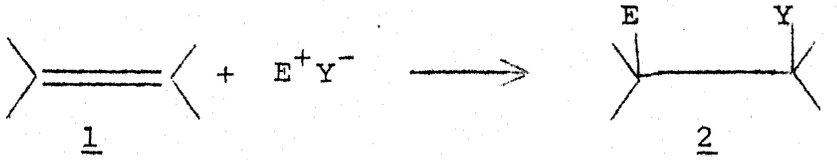
I.1 ABSTRACT

Electrophilic addition of iodine azide, mercuric acetate, benzenesulphenyl chloride, nitrosyl chloride and diborane to tricyclo[4.2.2.$O^{2,5}$]deca-3,7-diene derivatives 57, 58 and 59 is described. Reaction of iodine azide with diester (57) furnishes a cis azido iodide (63). This to our knowledge is the first example of stereospecific cis-addition of IN_3 to an olefin. The IN_3 addition to 58 and 59 in acetonitrile solvent results in transannular solvent participation and tetrazoles (68) and (66) are formed via Hassner-Ritter reaction. On the other hand, in methylene chloride solvent, dienes 58 and 59 furnish the tetracyclic azido iodides (69) and (67). Methoxymercuration of 57, 58 and 59 with mercuric acetate yields the corresponding cis-oxymercurials 81, 87 and 88 in

high yield. Reaction of benzenesulphenyl chloride with dienes 57, 58 and 59 resulted in a nonstereospecific addition and a mixture of cis and trans adducts 100-105 are obtained in good yield. The structure and stereochemistry of all the addition products has been unambiguously deduced from analytical data and pmr spectroscopy. The exclusive cis addition of IN_3 and $Hg(OAc)_2$ to the cyclobutene double bond of tricyclo[4.2.2.$0^{2,5}$]deca-3,7-dienes is interpreted in terms of the dominant role of twist strain theory. The nonstereospecific addition of benzenesulphenyl chloride is best interpreted in terms of a carbonium ion intermediate. The long range effect of substituents at C_9 and C_{10} on the reaction rates and product formation is also discussed.

I.2 INTRODUCTION

One of the most common and extensively investigated reaction of olefins is the addition of electrophiles. In this addition a double bond is attacked by an addendum to form an adduct in which both the atoms of the unsaturated bond have become saturated by the formation of covalent bonds. Using this definition, the reaction of a hypothetical electrophile ($E^+ Y^-$) with an alkene (1) to give an adduct (2) is an electrophilic addition reaction (Eq. 1):



1 2 ..(1)

The chemical literature[1-6] abounds with examples of addition of a wide array of electrophiles (halogens, protic acids, metal salts etc) with myriad types of cyclic and acyclic olefins. Many of these reactions have been the source of interesting molecular rearrangements[7] and find useful applications in organic synthesis.[8] Over the years, considerable effort has been expended by organic chemists to elucidate the mechanism[3] and stereochemistry[4,5] of electrophilic additions. Despite these extensive investigations, an all encompassing mechanism which also accounts for the observed stereochemistry is not available. Several recent review articles[3-5] provide authoritative and comprehensive account of the mechanism and stereochemistry of electrophilic additions and focus attention to the ambiguities that currently exist in literature. As the results described in this chapter deal with the mechanistic and stereochemical aspects of electrophilic additions, a brief coverage of related literature is provided to serve as the background material. This introduction is therefore intended to be a critical summary rather than a comprehensive account.

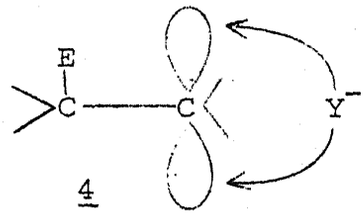
The three limiting mechanisms for electrophilic additions that have been often quoted in the literature[1,3,6] and find support through extensive kinetic and product analysis studies are the bimolecular addition ($Ad_{E}2$), the termolecular addition ($Ad_{E}3$) and the molecular addition ($Ad_{E}2M$). Among these the two step $Ad_{E}2$-type addition proceeding <u>via</u> a

carbonium ion intermediate has been the one most commonly encountered. In this process, a rate limiting attack of the electrophile on olefin furnishes an intermediate (3) which rapidly collapses to the product (Eq. 2). Depending upon the electrophile and substrate structure, the intermediate cation (3) can have either an open or bridged structure. If the cation (3) has an open carbonium ion structure 4, a non-

$$\text{Olefin} + E^+Y^- \xrightarrow{\text{slow}} \underset{3}{[\text{Olefin } E]^+} + Y^- \xrightarrow{\text{fast}} \text{Olefin EY} \quad \ldots (2)$$

$Ad_{E}2$ Mechanism

stereospecific addition results and a mixture of cis and trans products is obtained. On the other hand, the intermediate can have a bridged or onium ion structure 5 and thus lead stereospecifically to trans-addition via a process reminiscent of the S_N2 displacement reaction.



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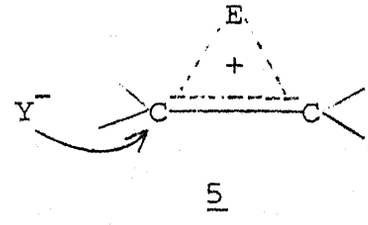

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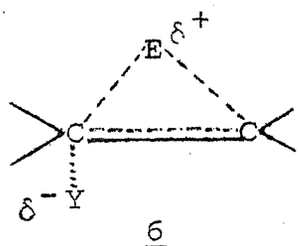
In fact, most electrophiles like chlorine, bromine, iodine azide,[9] sulphenyl halides[10] and mercuric salts[11-13] having the ability to stabilise the neighbouring carbonium ion react with simple olefins via this latter process and result in stereospecific trans-addition. This preference for stereospecific trans-addition has been attributed to the fact that

the trans coplanar transition state (6) is lower in energy than the corresponding cis transition state (7).[6,14*]



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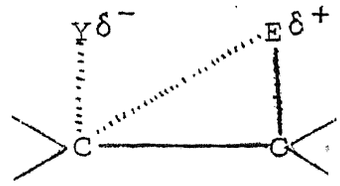

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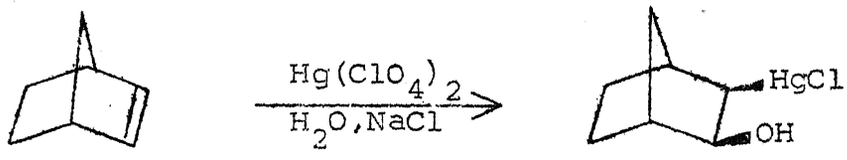
In 1959, Traylor and Baker[15] reported the discovery that the addition of mercuric salts to bicyclo[2.2.1]hept-2-ene (norbornene, 8) resulted in stereospecific exo,cis-addition and the hydroxymercurial (9) was the sole product of the reaction. In this reaction, neither any trans-addition nor any



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rearrangement product was encountered. This significant observation stirred up a flurry of activity in the area of electrophilic additions to norbornene (8) and related olefinic systems on several counts. Firstly, the results of Traylor and Baker[15] were contrary to expectation (in view of the known trans-oxymercuration of simple alkenes) and secondly, the norbornyl system (and norbornene) was at that time the focal point of nonclassical vs classical carbonium ion controversy. In the early sixties, several research

*We have used terms "cis-addition" and "trans-addition" throughout this chapter in preference to "syn- and anti-addition" so as to have common terminology for the stereochemistry of addition as well as that of adducts and substrate.

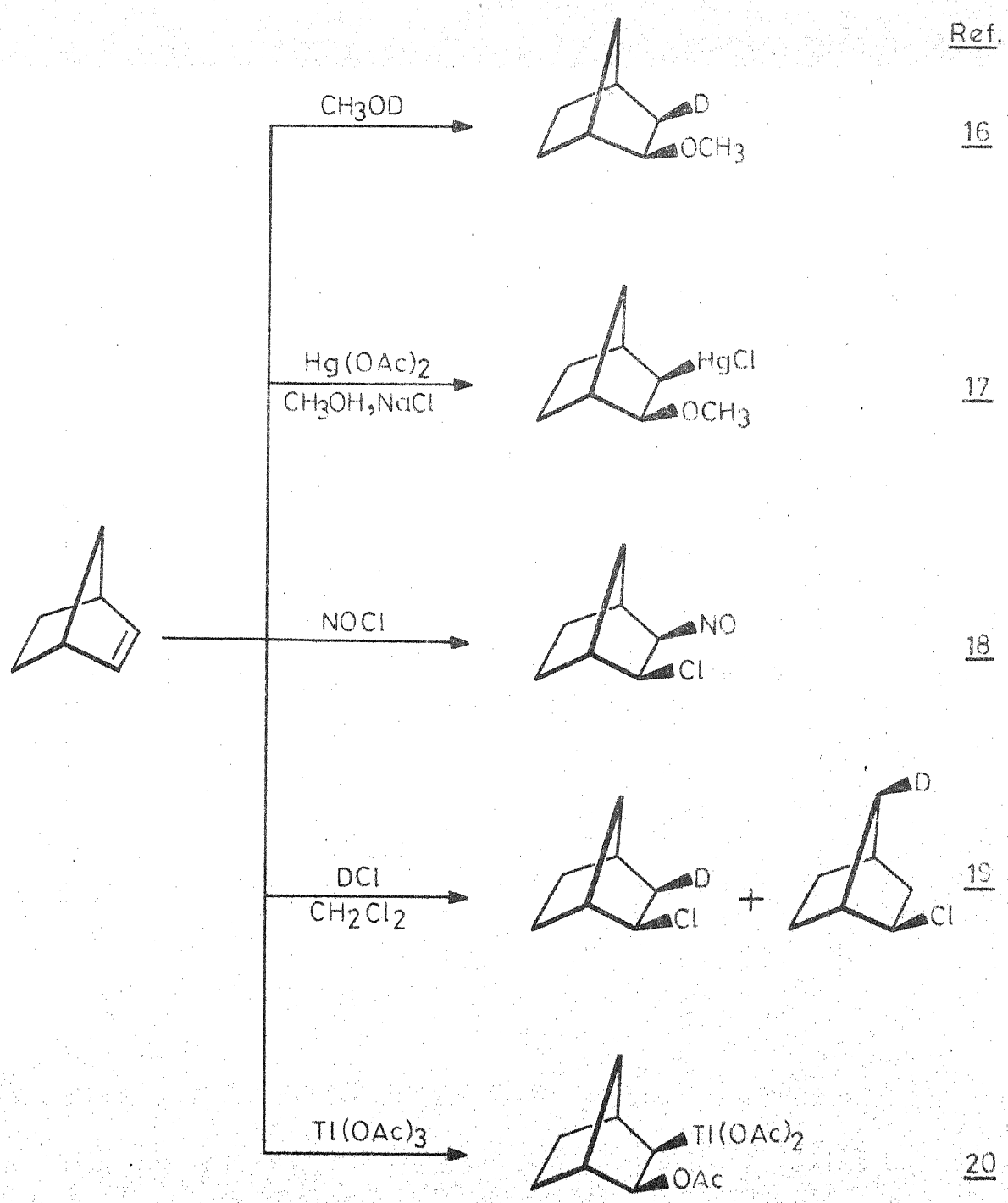
groups led by Professors Winstein, Cristol, Traylor and Meinwald reported[15-20] in rapid succession the stereospecific exo,cis-addition of assorted electrophiles to norbornene (8) and the results are summarised in Scheme I.1. It was observed[20-24] that many other bi- and tricyclic olefins possessing a strained double bond also undergo stereospecific cis-additions and some selected examples are provided in Scheme I.2.

Since, the stereospecific cis-additions (Schemes I.1 & I.2) were inexplicable in terms of the ordinary two step mechanism (cf. trans-addition with simple olefins), the need for an alternate explanation became quite evident and several theories have been proffered to account for these observations. As the early examples[15-20] of cis-additions emanated from bicyclo-[2.2.1]heptene chemistry, the first attempts to rationalise these results were naturally influenced by the nonclassical vs classical carbonium ion formulations.[25-27] A brief, up-to-date account of the various explanations, based on electronic, conformational and geometrical constraints is described here. However, it will be quite apparent from the discussion presented here that none of the theories is entirely satisfactory and several inconsistencies remain to be explained.

Nonclassical Carbonium Ion Formulation (σ-Participation[25-27])

This explanation relates the exo,cis-addition of electrophiles to norbornene (8) with the preferred exo attack of

Scheme I.1


Ref.
CH3OD
D
OCH3
16
Hg(OAc)2
CH3OH,NaCl
HgCl
OCH3
17
NOCl
NO
Cl
18
DCl
CH2Cl2
D
Cl
+
D
Cl
19
Tl(OAc)3
Tl(OAc)2
OAc
20

Scheme I.2

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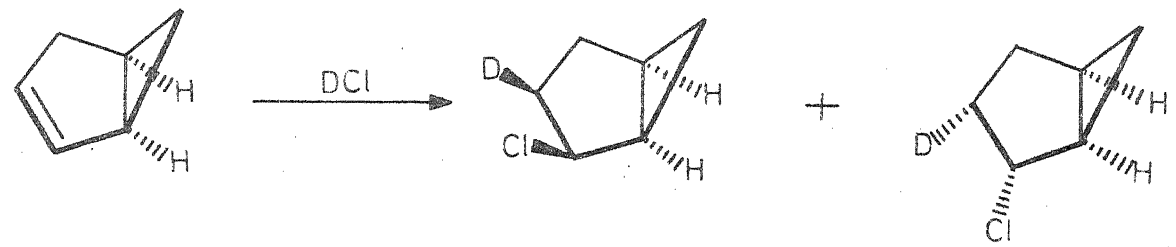

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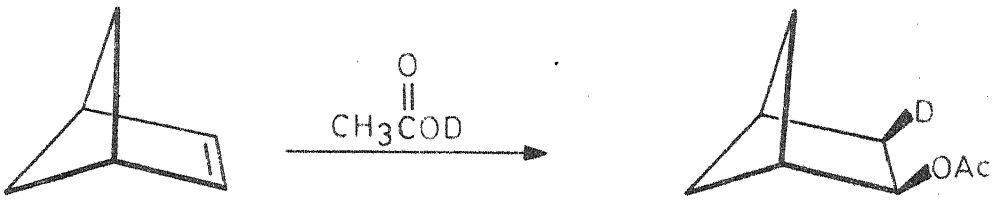

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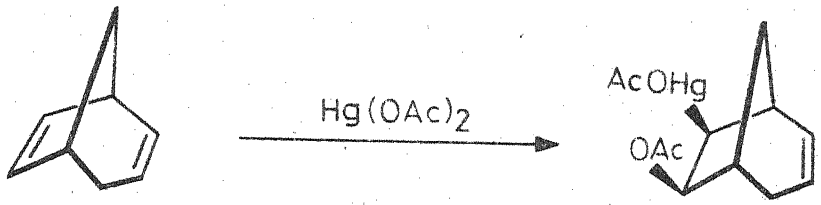

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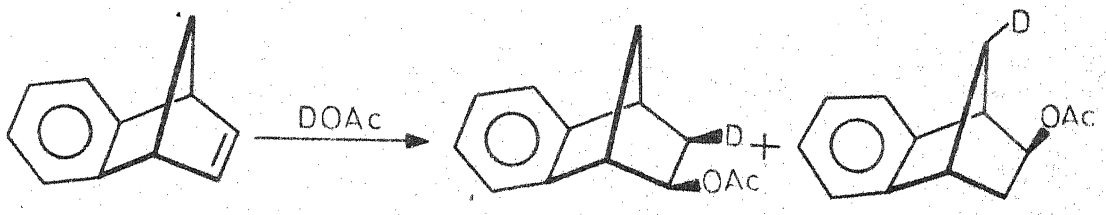

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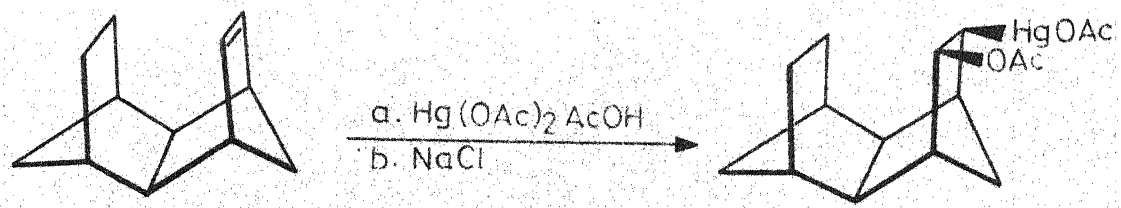

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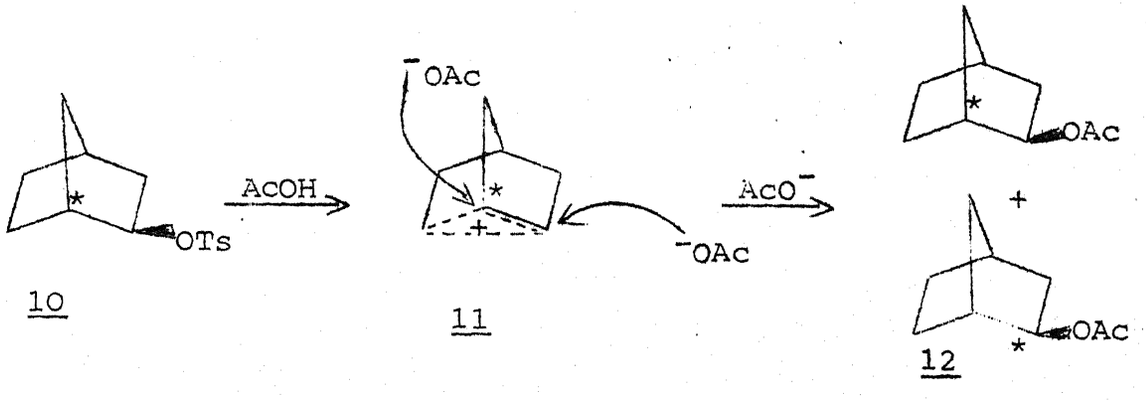
nucleophiles on the norbornyl cation. It is well known[27,29] that acetolysis of norbornyl tosylate (10) furnishes exclusively the exo-acetate (12) with complete racemisation and scrambling of C_1 and C_2 carbon atoms (Scheme I.3). Winstein and coworkers[29] proposed that the solvolysis of tosylate (10) proceeds with participation of C_1-C_6 bonding pair to produce a resonance stabilised cationic intermediate, possessing the σ- bridged structure 11. The symmetrical ion (11) can only accept nucleophiles from the exo face as the endo side is hindered by the delocalised σ electron cloud. A wealth of evidence, including the recent pmr,[30,31] cmr,[31] Raman[32] and ESCA[33,34] studies on stable 2-norbornyl cation, supports the bridged ion proposition. If this formulation is accepted, then the addition of electrophile (E^+Y^-) to norbornene (8)

Scheme I.3

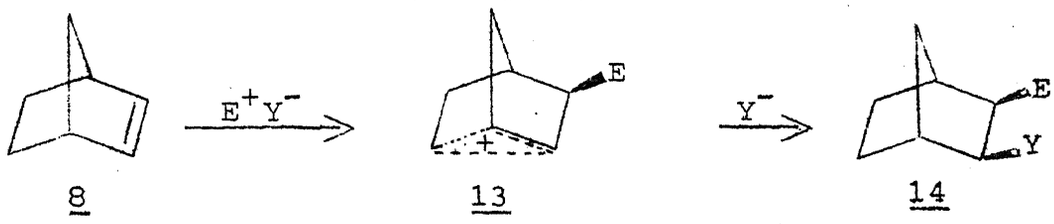


10 11 12

will produce a bridged ion (13) via exo attack of E^+ and C_1-C_6 σ participation in the transition state. The addition of Y^- to (13), also from the exo face will then result in overall cis-addition to furnish 14. Alternatively, attack of

Y^- at C_1 would lead to the rearrangement product 15 (Scheme I.4):

Scheme I.4



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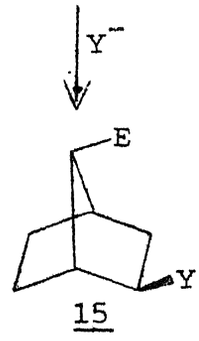

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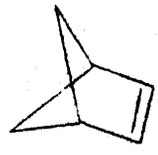
Although, nonclassical ion formulation provides a reasonable rationale for the cis,exo-addition in norbornyl system, it can not be invoked, for several reasons, to explain cis-addition to other bi- and tricyclic olefins. For example, the geometry of both bicyclo [2.1.1] hex-2-ene (16) and bicyclo-[2.2.2] oct-2-ene (17) is not favourable for σ participation to give intermediates (18) & (19), yet both of these olefins undergo stereospecific cis addition.



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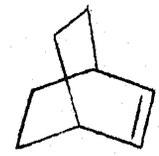

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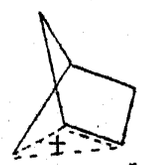

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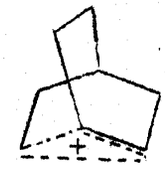
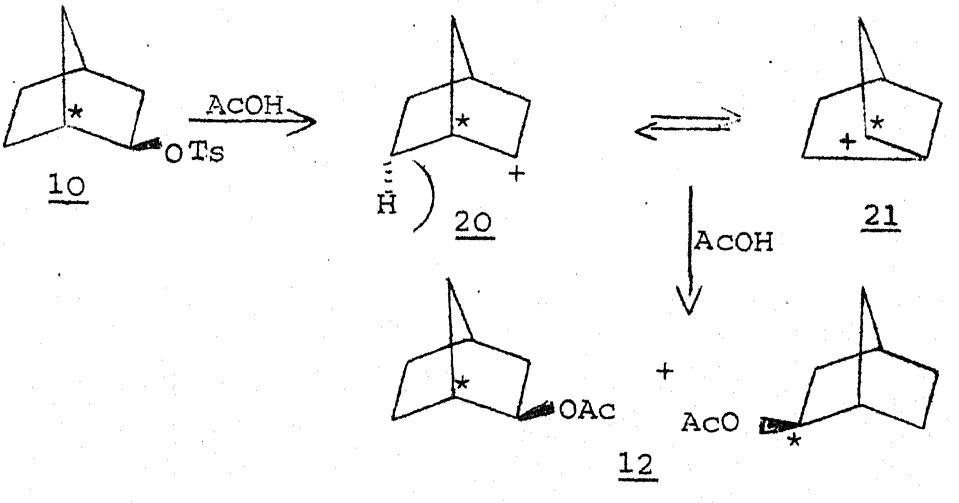


19

Equilibrating Classical Ions and Steric Control

On the basis of extensive experimental evidence, Professor H.C. Brown has seriously questioned[28,35] the contention that exo selectivity of 2-norbornyl cation is due to σ participation and intervention of nonclassical ion (11). He contends that this preferred exo attack is a consequence of steric control, as the approach of the reagent to the trigonal centre at C_2 in bicyclo [2.2.1] heptyl system is sterically hindered from the endo side by the C_6 endo hydrogen atom. Furthermore, the racemisation, rearrangement and scrambling of C_1 and C_2 in the solvolysis of norbornyl tosylate (10) can be readily explained[28] in terms of equilibrating classical ions (20) & (21) and thus there is no need for a "special" interpretation (Scheme I.5):

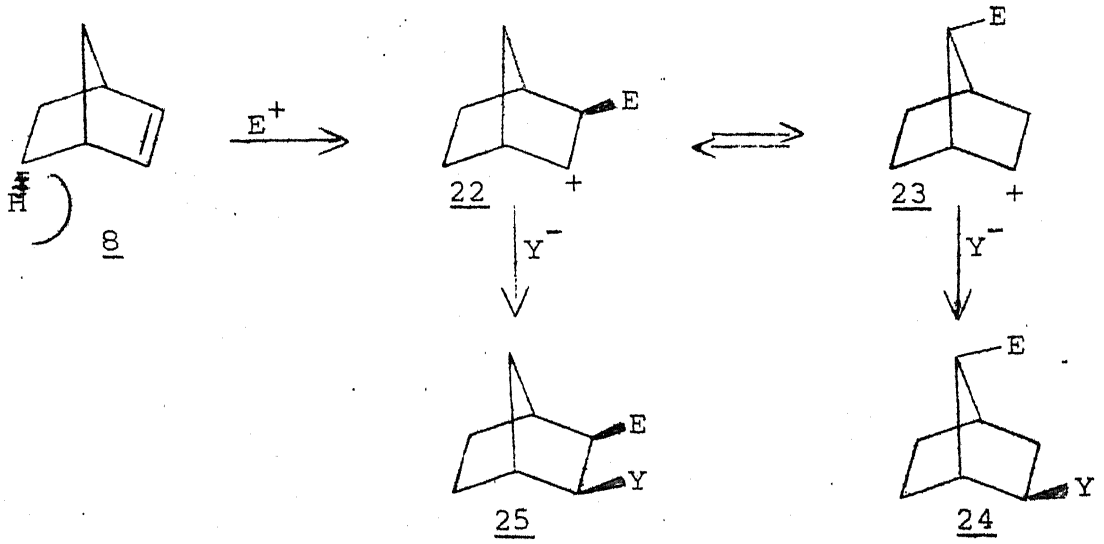
Scheme I.5



Extension of the steric control idea would require that both E^+ and Y^- must add to norbornene (8) from the less hindered exo face only (Scheme 1.6). Thus, the equilibrating pair of

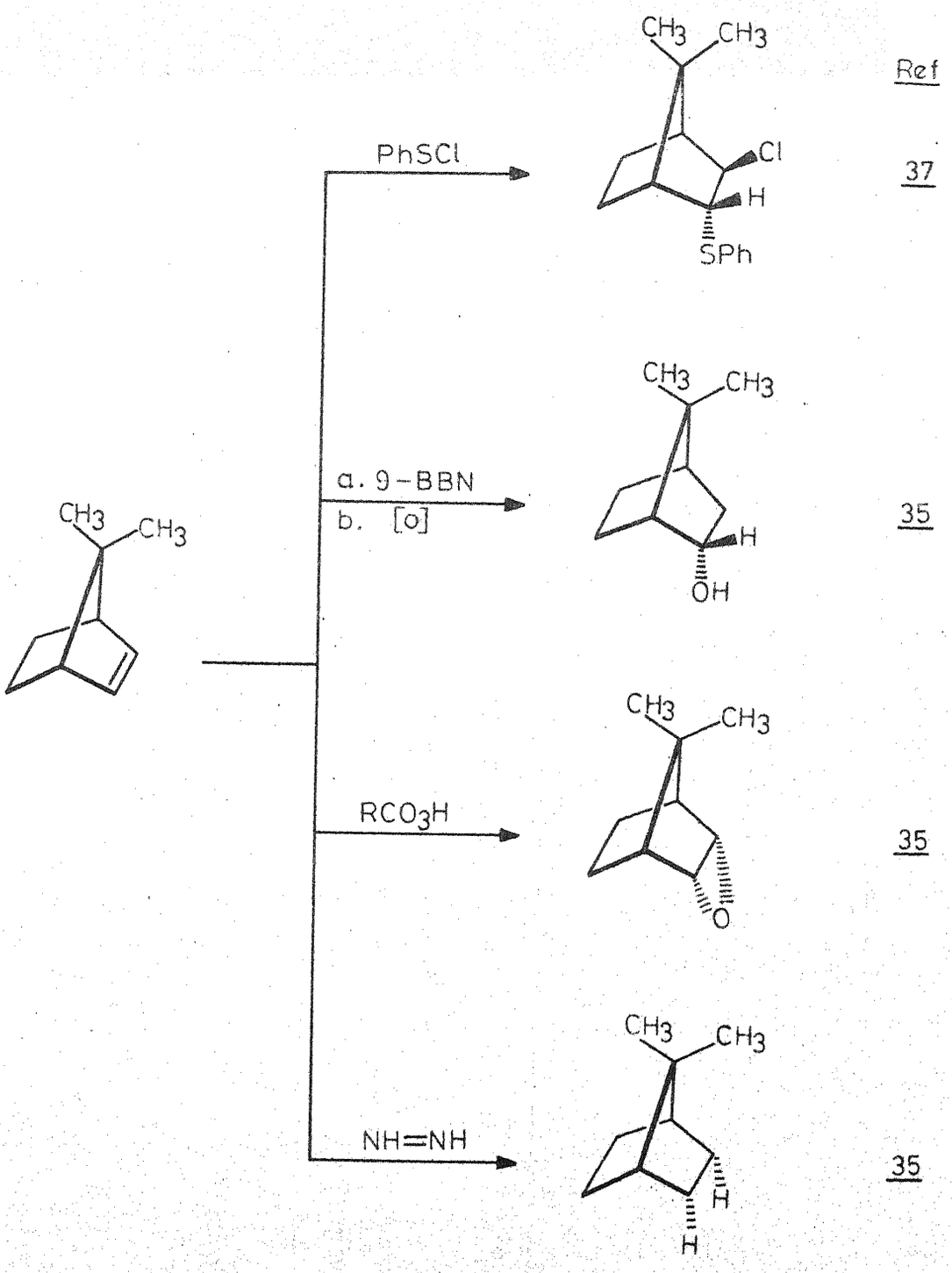
ions (22) & (23) formed by the addition of E^+ to 8 can account for the rearrangement to 24 and cis-addition to 25.

Scheme I.6



However, there are several experimental observations that can not be fully reconciled to the steric control arguement. Firstly, several norbornene derivatives in which the exo face is more hindered due to the presence of 7,7-dimethyl substituent undergo exclusive exo,cis-oxymercuration[35,36] and deuterium chloride[19] addition (Scheme I.7). On the other hand, the presence of the 7,7-dimethyl substituent does bring about, in some cases, reversal[35,37] in the stereochemistry of addition to norbornene from preferred exo to endo (Scheme I.8). Brown has attempted to explain[35] these results in terms of the nature of the electrophilic addend and the mechanism of addition. It is proposed[35] that in single-stage electrophilic additions (e.g., hydroboration, epoxidation, benzenesulphenyl

Scheme 1.8



Ref

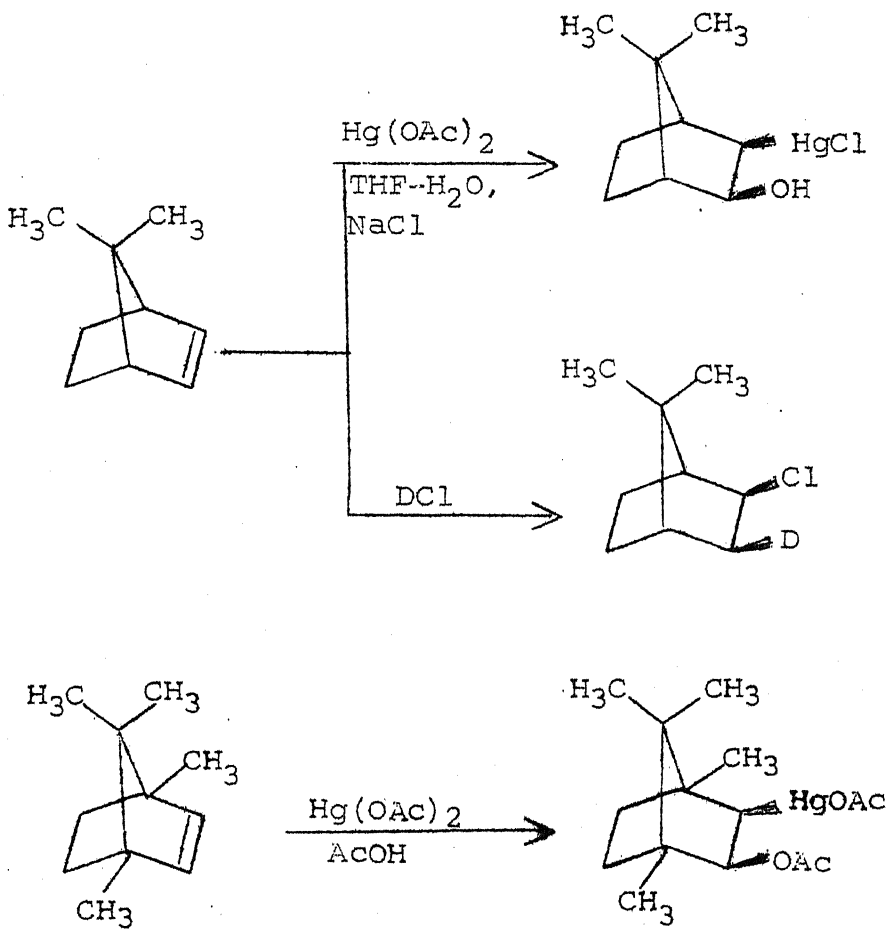
37

35

35

35

Scheme I.7

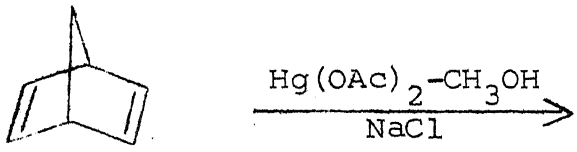


chloride addition and hydrogenation, Scheme I.8) proceeding via a cyclic intermediate, the attacking reagent is placed in the vicinity of 7,7-dimethyl group and thus an endo-addition is preferred. However, two stage additions (e.g., oxymercuration, hydrochlorination etc, Scheme I.7) proceeding via a carbonium ion intermediate are insensitive to the 7,7-dimethyl group as the reagent can manoeuvre an exo approach to the p orbital from the corners of the bicyclic structure. Unfortunately, it is assumed in this explanation that

oxymercuration is a two stage reaction, inspite of the widely held view[38-40] that mercurinium ions are intermediates in these additions.

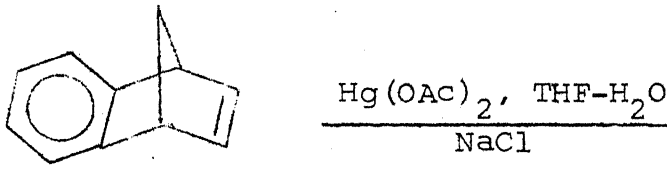
The second major difficulty with the steric control theory is that norbornadiene[41,42] (26) and benzonorbornadiene[43] (27) lacking C_6 endo hydrogens furnish exclusively cis,exo-adducts (28) & (29) on oxymercuration (Scheme I.9).

Scheme I.9



Ref. 41,42

26 28



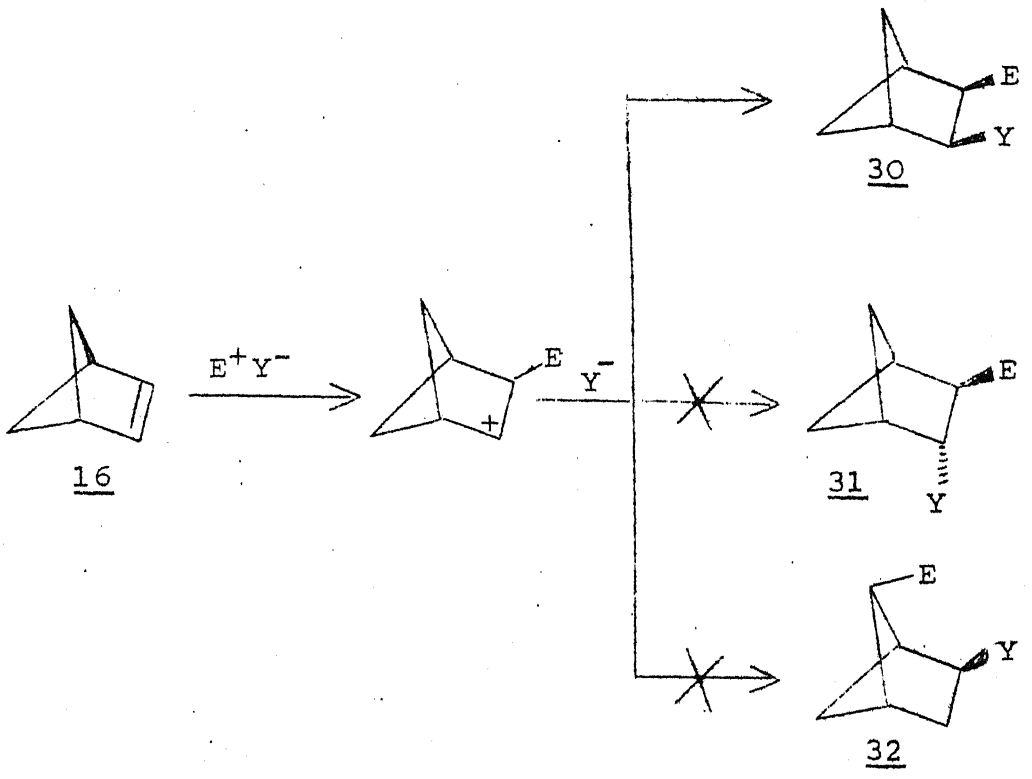
Ref. 43

27 29

Furthermore,symmetrical olefins like bicyclo[2.1.1]hex-2-ene (16) furnish only cis product 30 and no trans-adduct 31 or rearrangement product 32 is encountered[22] (Scheme I.10).

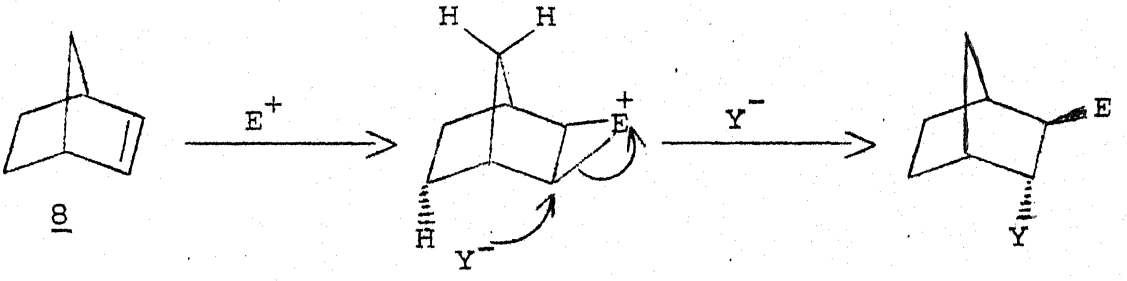
Finally, trans-addition of bromine[44,45] or benzenesulphenyl chloride[46] to norbornene (8) requires approach of the nucleophile (Y = Cl or Br) from the endo side (33,

Scheme I.10



E = S-Ph, Br). The three membered ring in onium ion (33) is likely to be tilted away from the methylene bridge (perhaps enhancing the steric interference from C_6 endo hydrogen towards endo attack at C_2) and yet endo nucleophilic (Y = Cl or Br) addition 34a,b occurs (Scheme I.11). Therefore endo

Scheme I.11



33, E = S-Ph or Br

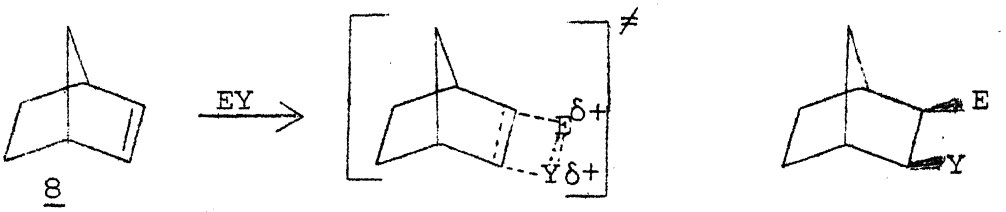
34a, E = S-Ph, Y = Cl
b, E = Y = Br

attack in norbornyl systems is certainly not prohibited.

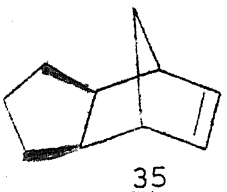
Molecular Electrophilic Addition

The simplest mechanism that can account for the cis-addition of an electrophile (E^+Y^-) to an olefin is a four centered cyclic addition (Scheme I.12). Meinwald has proposed[18] such a process to account for the cis-addition of nitrosyl chloride to norbornene (8, Scheme I.1). Similarly, cyclic addition of molecular hydrogen chloride to 8 has also been postulated.[21,47] Cristol and coworkers[48-50] have studied the acid catalysed addition of deuterated methanol, acetic acid and water to exo (35) and endo-trimethylene-norbornene (36) and found that products 37 and 38 of exo,cis-addition were formed. It was also observed that 35 & 36 gave a different mixture of products 37 & 38 during the addition reaction and thus the σ-bridged nonclassical ion (39) could not be the common, sole product forming species in both the cases. These observations have been rationalised by Cristol[48-50] in terms of a mechanism involving the ion (39) in competition with a molecular cis-addition. Many other cis-additions have also been explained[4] in terms of this molecular addition process. However, it remains to be explained as to why only strained olefins like norbornene (8) undergo such molecular additions. Also, orbital symmetry considerations[51] do not permit a concerted four centred cis-addition.

Scheme I.12



8 14



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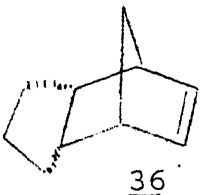

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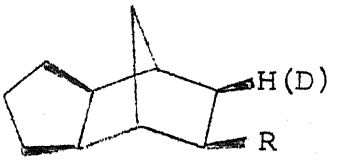
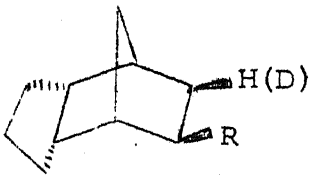
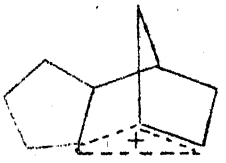


37, R=OCH_3, OAc, OH



38, R=OCH_3, OAc, OH



39

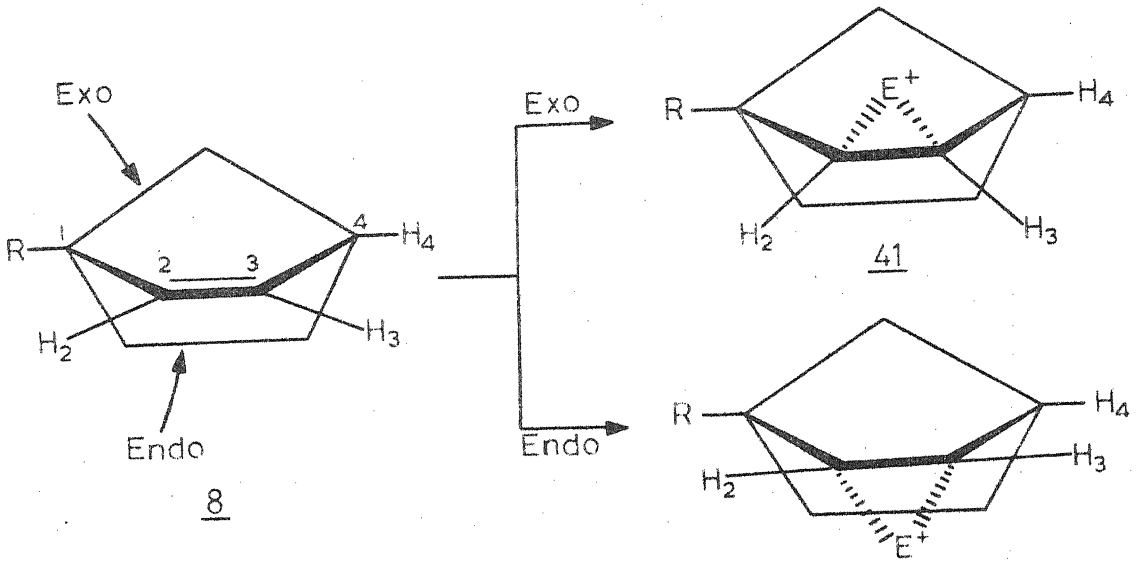
Torsional Effects

It was proposed by Schleyer[52] in 1967 that the exo-selectivity exhibited in many different reactions by various norbornyl derivatives could be ascribed, at least in part, to the torsional strain arising from the eclipsing interactions with bridehead substituents. The effect can be

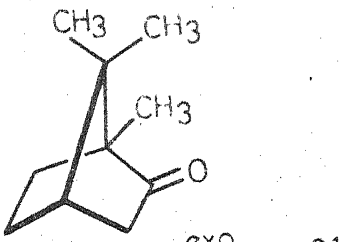
clearly visualised by examining the special geometry around the C_1-C_2 bond in bicyclo[2.2.1]heptene (8) or 2-norbornyl-cation (Scheme I.13). An *endo* attack by an electrophile upon norbornene (8) would cause the eclipsing of the C_2-H_2 bond with C_1-H_1 bond and of C_4-H_4 bond with C_3-H_3 bond *40*. On the other hand, an *exo* attack would lead to a staggered conformation *41* across C_1-C_2 and C_3-C_4 bonds. The energy difference between the two modes of addition *40* & *41* is probably enough to account for the preferred *exo*-addition. Schleyer's theory[52] is quite plausible and has been used in the interpretation[53-57] of a variety of data but independent experimental tests have failed to produce unambiguous evidence in its support. A few instances may be cited here.

An obvious probe to gauge the effectiveness of torsional effects in norbornyl systems would be to magnify them by placing bulky substituents in 1-position. Tidwell[58] studied the rate of *exo*/*endo* deuterium exchange (acceptance of the proton by the enolate from *exo* side) in ketones (42) & (43) and found them to be quite comparable. Also, base catalysed equilibration studies with 1-substituted *exo* and *endo* norbornane derivatives (44) and (45) by Mellor[59] lead to the conclusion that torsional effects, if operative in such systems, are either minor or are obscured by other factors. Furthermore, bicyclo[2.1.1]hexene (16) and bicyclo-[2.2.2]oct-2-ene (17) are symmetrical about the double bond and therefore torsional effects for *cis* or *trans*-addition

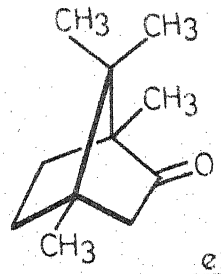
Scheme I.13



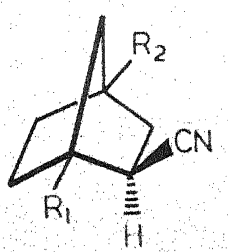
8 41 40



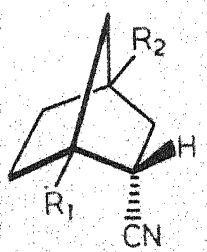
42 $\frac{exo}{endo} = 21$



43 $\frac{exo}{endo} = 19$



44 a. $R_1 = CH_3, R_2 = H$
b. $R_1 = H, R_2 = CH_3$

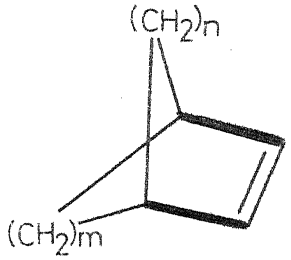


45 a. $R_1 = CH_3, R_2 = H$
b. $R_1 = H, R_2 = CH_3$

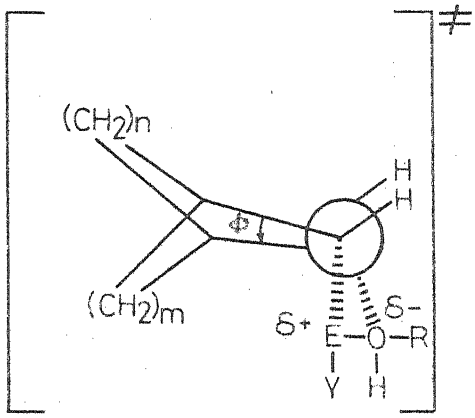
should be identical. But both 16 and 17 undergo stereospecific cis-additions.

The Twist Strain Theory

A perusal of experimental results on electrophilic additions reveal that cis-additions are generally encountered in strained rigid olefins. This led Traylor[5] to suggest that the stereospecificity in these additions might be a consequence of geometrical constraints imposed by the olefin structure. This is clearly borne out by a consideration of the transition states (47) & (48) for cis- and trans-additions to bicyclic olefin (46). It is evident that the trans addition (48) provides the ideal staggered arrangement of groups as compared to the cis-addition (47) in which eclipsing of two sets of bonds occurs. If no other constraints are imposed, trans-addition (48) will be favoured as is often the case with numerous cyclic and acyclic olefins. However, if n and m in olefin (46) have the values 1 and/or 2, the two bridgehead bonds (marked with heavy line) are held in eclipsed configuration and any rotation away from this eclipsed state would cause severe strain in the bicyclic structure (see, angle ∅). The transition state for trans addition (48) requires staggering of the eclipsed bridgehead bonds and this imposes prohibitive strain on the geometry of the bicyclic framework. Thus, cis transition state (47) in which eclipsing of bridgehead bonds is essentially

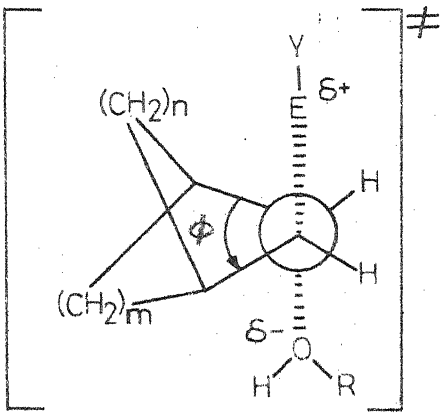


46



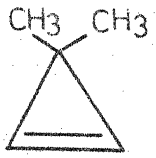
ts for cis addition

47

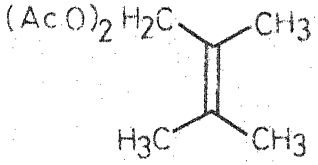


ts for trans addition

48

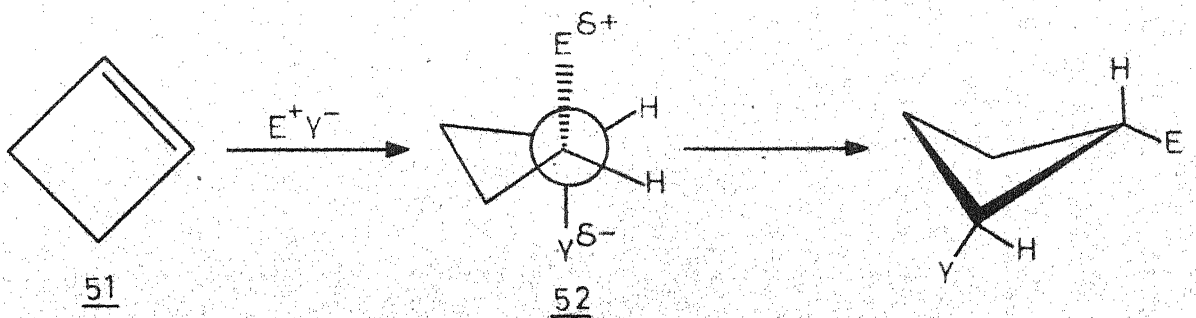


49



50

Scheme 1.14



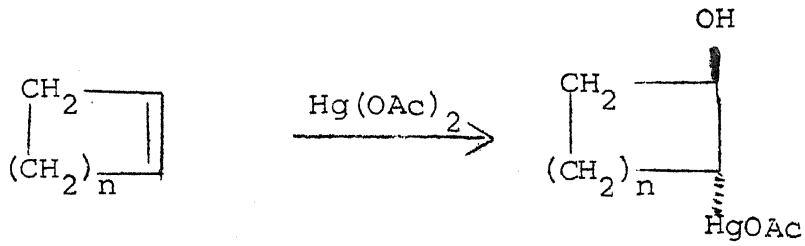
51

52

retained, will be preferred for the addition of electrophiles.

The twist strain concept proposed by Traylor[5] is an attractive one, as it is not related to the exo-preferences in norbornenes and thus steers clear of the vexatious classical vs nonclassical ion problem.[25-28] An independent evaluation of twist strain factors can be obtained by the study of electrophilic additions to cyclopropenes and cyclobutenes. If twist strain factors are dominant, it can be predicted that cyclopropenes and possibly cyclobutenes must add electrophiles in a cis manner as the transition state for trans-addition will be extremely strained. Unfortunately, addition of electrophiles to cyclopropene derivatives results in a facile ring opening reaction. A recent example[60,61] of oxymercuration of cyclopropene derivative (49) to diacetate (50) illustrates their general mode of reaction with electrophiles. On the other hand, cyclobutene (51) though flat would tend to attain the puckered conformation of cyclobutane during the transition state (52) of electrophilic addition(Scheme I.14). This puckering (or twist) of the cyclobutane is sufficient to favour a trans-addition. In fact, cyclobutene[40,62] (51) like other C_5-C_8 cyclic alkenes[62-64] (53) has been shown to oxymercurate in trans fashion 54 (Scheme I.15). However, only a few examples of electrophilic addition to cyclobutene are reported in literature.

Scheme I.15



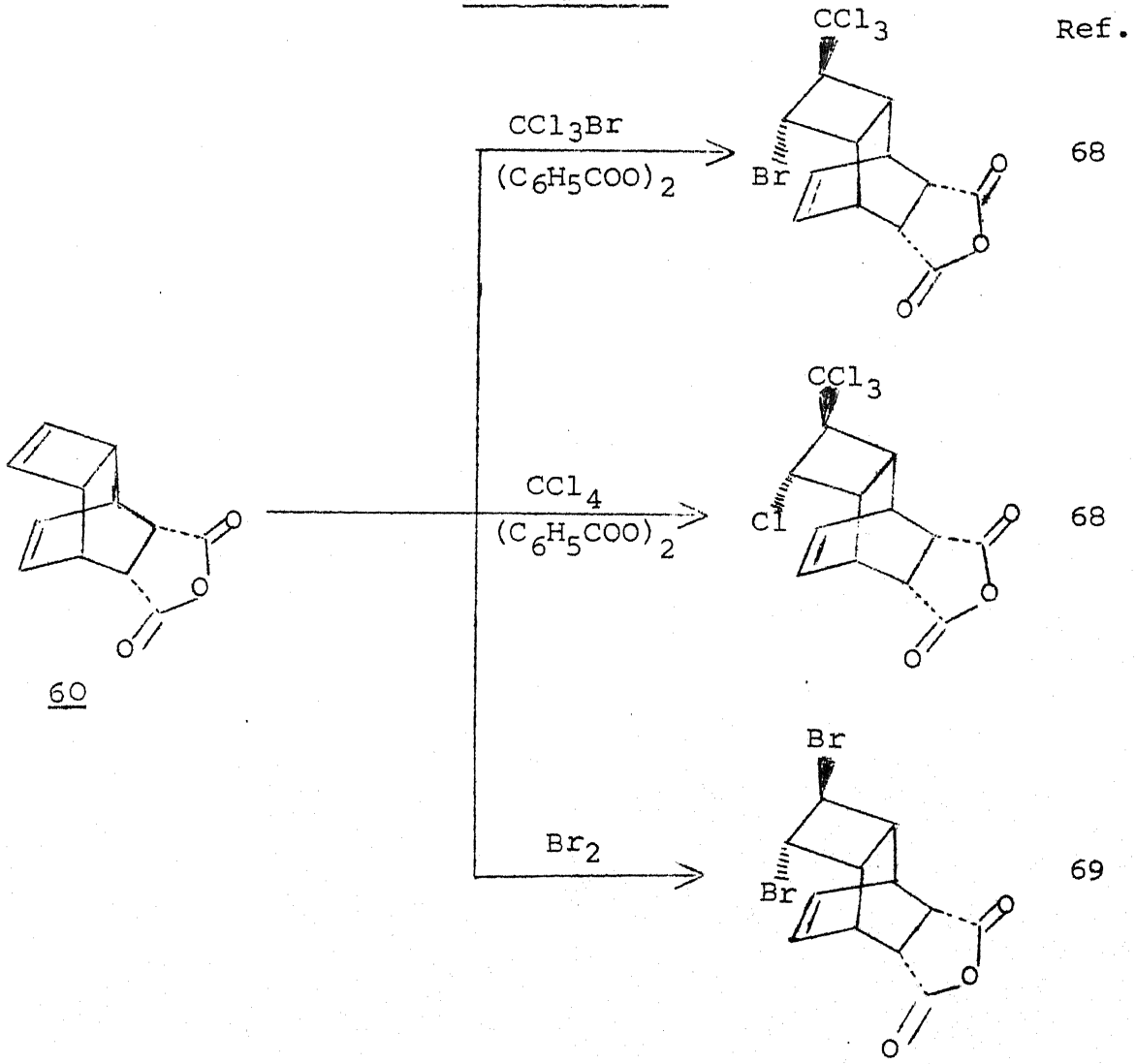
53, n = 1-4 54, n = 1-4

It appeared to us that a fused cyclobutene, which is part of a rigid framework, would undergo cis-electrophilic addition as the conformational flexibility of a simple cyclobutane will no longer be available to it in the transition state. Such a cyclobutene, in our opinion would be the substrate of choice for assessing twist strain effects. Consequently, efforts were directed towards the selection of a suitable 'rigid' cyclobutene derivative.

The tricyclo [4.2.2.$0^{2,5}$] deca-3,7-diene ring system 55, readily available from cyclooctatetraene (56) via the diene synthesis,[65,66] is endowed with a unique geometrical disposition of a strained cyclobutene double bond and a sterically shielded cyclohexene moiety, ideally suited for the study of electrophilic additions and transannular reactions. Moreover, the variation of substituents (R) at C_9 and C_{10} in 55 without altering the geometrical relationship of the double bonds provides an interesting variant for the study of long range electronic effects. Another advantage of the ring system 55 is the availability of a simple and reliable

pmr method[67] for the determination of stereochemistry of the substituents on the cyclobutene ring. An examination of molecular models as well as reported chemistry of 55 convinced us that there was no impediment to endo attack on the cyclobutene ring. In fact, several examples of endo attack on the cyclobutene ring of 55 have been recorded in literature[68,69] (Scheme I.16).

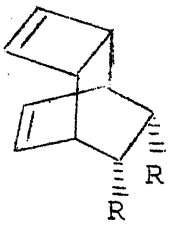
Scheme I.16



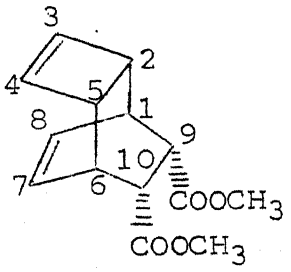
In the present investigation, three tricyclo$[4.2.2.0^{2,5}]$-deca-3,7-diene derivatives namely, diester (57), tetracyclic ether (58) and the dimethyl compound (59) were chosen as the substrates for the study of electrophilic additions. In these compounds, the geometrical disposition of the double bonds and reacting site remains the same, while the availability of π electrons for participation by the C_7-C_8 double bond is altered due to the presence of electron withdrawing and donating groups at C_9 and C_{10} *endo* position. The electrophiles selected for the present study were iodine azide,[9] mercuric acetate,[11] benzenesulphenyl chloride,[10] nitrosyl chloride and diborane. Among them, iodine azide and benzenesulphenyl chloride were of particular interest because of their known[9,11] propensity for *trans*-addition *via* the corresponding onium ion intermediates.

In this chapter of the thesis, the results of addition of several electrophiles like, iodine azide, mercuric acetate, benzenesulphenyl chloride etc, to the tricyclo-$[4.2.2.0^{2,5}]$-deca-3,7-diene derivatives *57*, *58* & *59* are described. The mechanistic and stereochemical aspects of these additions are discussed. The effect of variation of substituents at C_9 and C_{10} on the reaction rates and product formation is also reported.

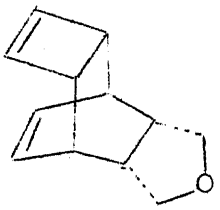
56



55



57



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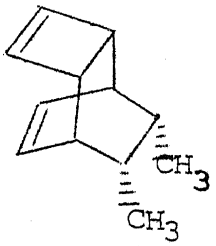
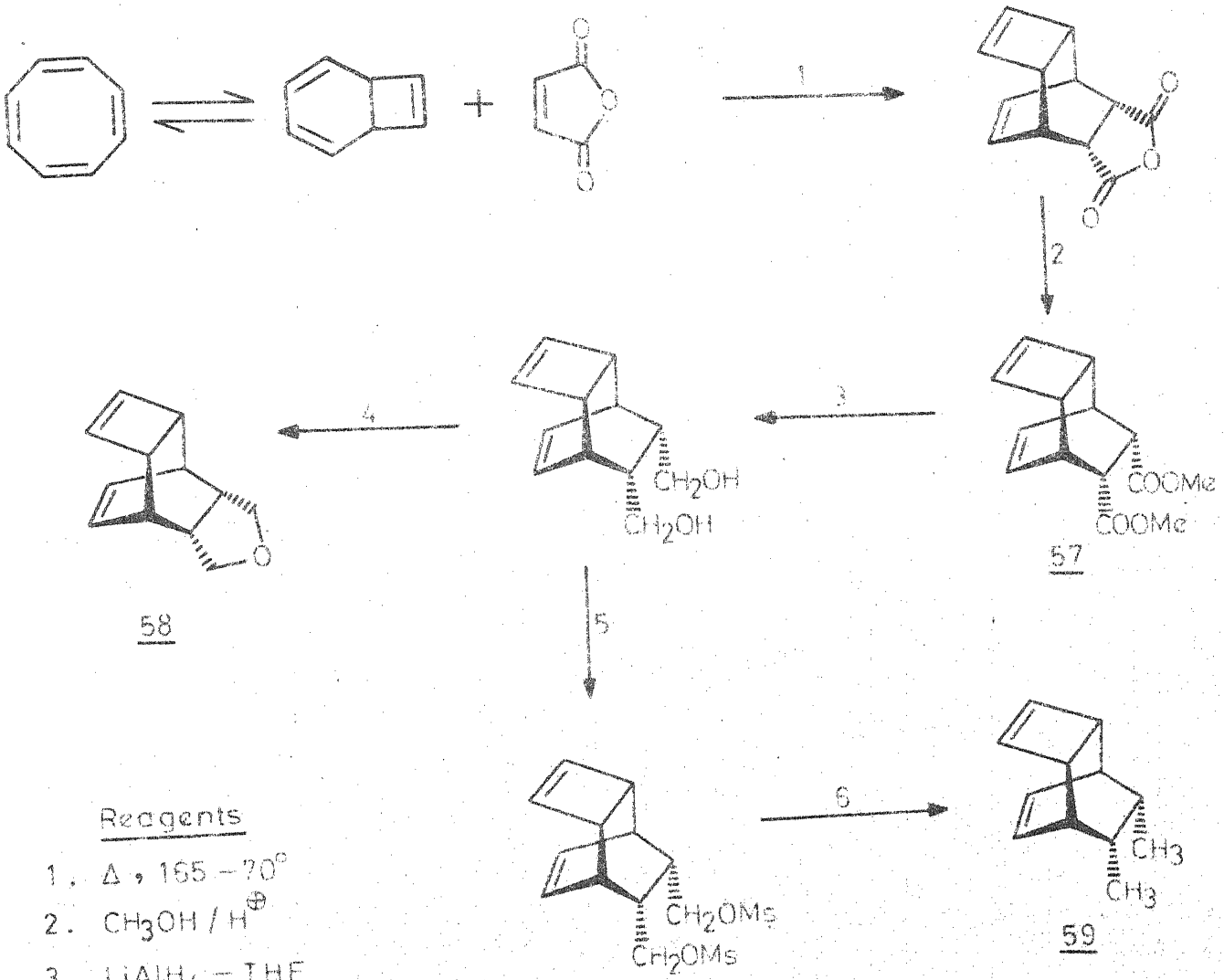


59

I.3 RESULTS AND DISCUSSION

As already mentioned, tricyclo$[4.2.2.0^{2,5}]$deca-3,7-diene derivatives 57, 58 and 59 were selected for the contemplated stereochemical study of electrophilic additions. These substrates were readily synthesised from cyclooctatetraene maleic anhydride adduct[65] (60) via routine functional group transformations involving a slight modification of literature procedures.[70] The synthetic sequence is depicted in Scheme I.17 and details are provided in the experimental section. For the sake of convenient presentation, addition of each electrophile to the three substrates 57, 58 and 59 is described under separate heading. A brief discussion

Scheme 1.17



57 58 59

Reagents

1. Δ , 165 – 70°
2. CH_3OH / $H^{\oplus}$
3. $LiAlH_4$ – THF
4. Benzene /p-TsA
5. MsCl / Py
6. $LiAlH_4$ – THF

of the results has also been provided in each case.

Iodine Azide Additions

The reaction of diester (57) with IN_3 solution prepared *in situ* from excess of sodium azide and iodine monochloride in acetonitrile (-5°) according to the procedure of Fowler, Hassner and Levy[71] afforded a crystalline azido iodide (63), mp 137° in near quantitative yield. The structure of the IN_3 adduct follows from the diagnostic azide absorption at 2120 cm^{-1} and the ester bands at 1740 and 1210 cm^{-1} in the ir spectrum (Fig. I.1). The pmr spectrum (Fig. I.2) showed two quartets at δ4.32 and 3.50 due to tertiary protons attached to an iodo and azido group respectively, along with a clean triplet at δ6.51 due to the two olefinic protons. The *cis* orientation of I and N_3 substituents on the cyclobutane ring follows from the relatively sharp triplet for the two olefinic protons at C_7 and C_8 arising from the near equivalence of the vinyl hydrogens and the fortuitous near equivalence of their coupling constants. This assignment is further supported by the striking similarity of the olefinic proton signals in the azido iodide (63) (Fig. I.2) and the epoxide (65) (Fig. I.3), both of which bear symmetrical *endo* substitution. Furthermore, the 1,3-dipolar addition product 64, mp 192-4°, of 63 with dimethyl acetylenedicarboxylate also displayed, as expected, a sharp triplet at δ6.61 for the olefinic protons. The appearance

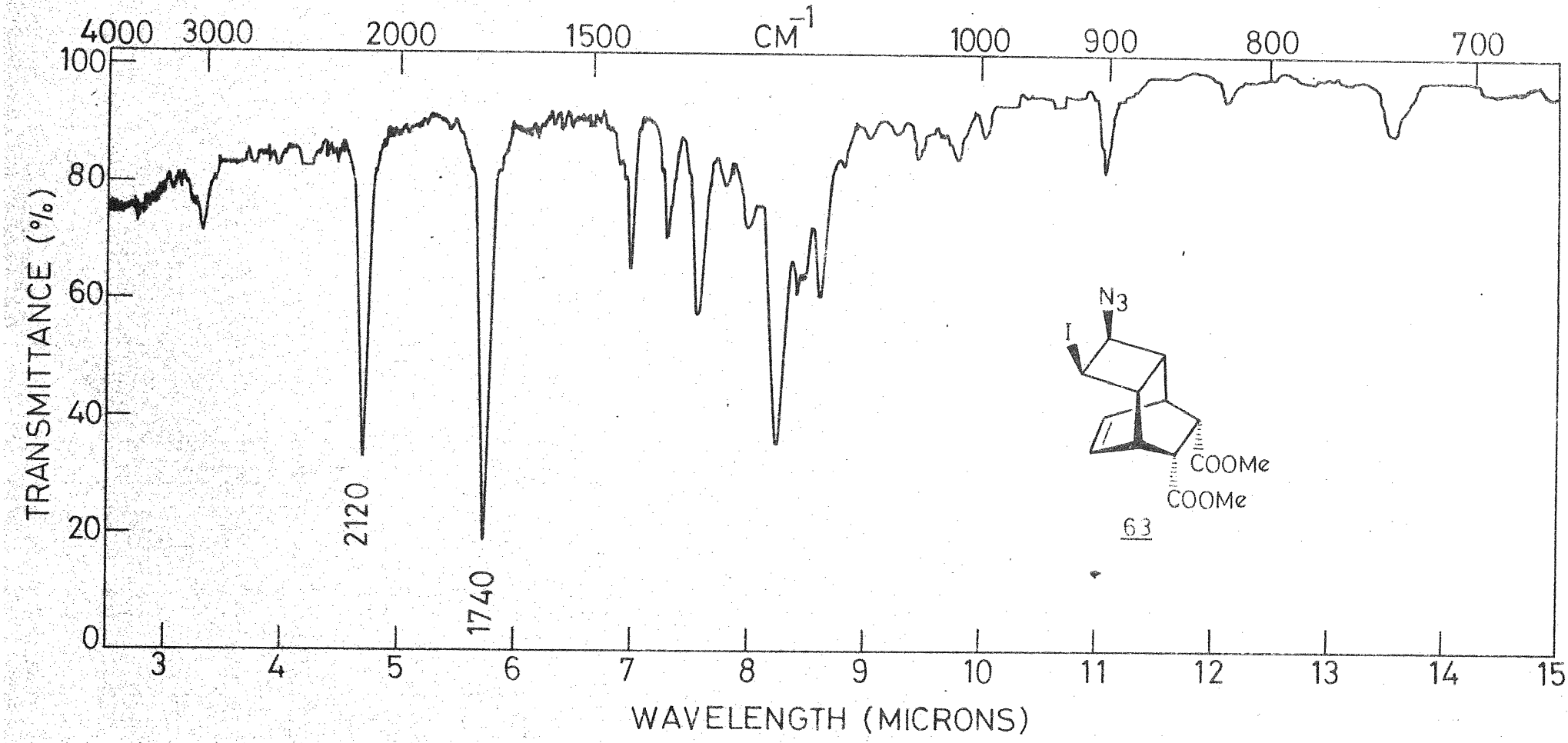
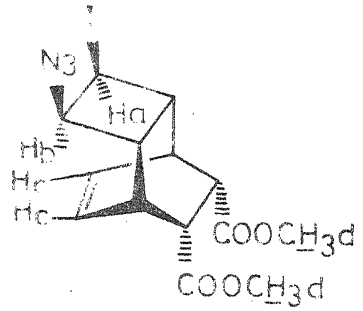


Fig. I.1 IR spectrum (KBr) of 63



63

Fig. I.2 PMR spectrum (60 MHz) of 63

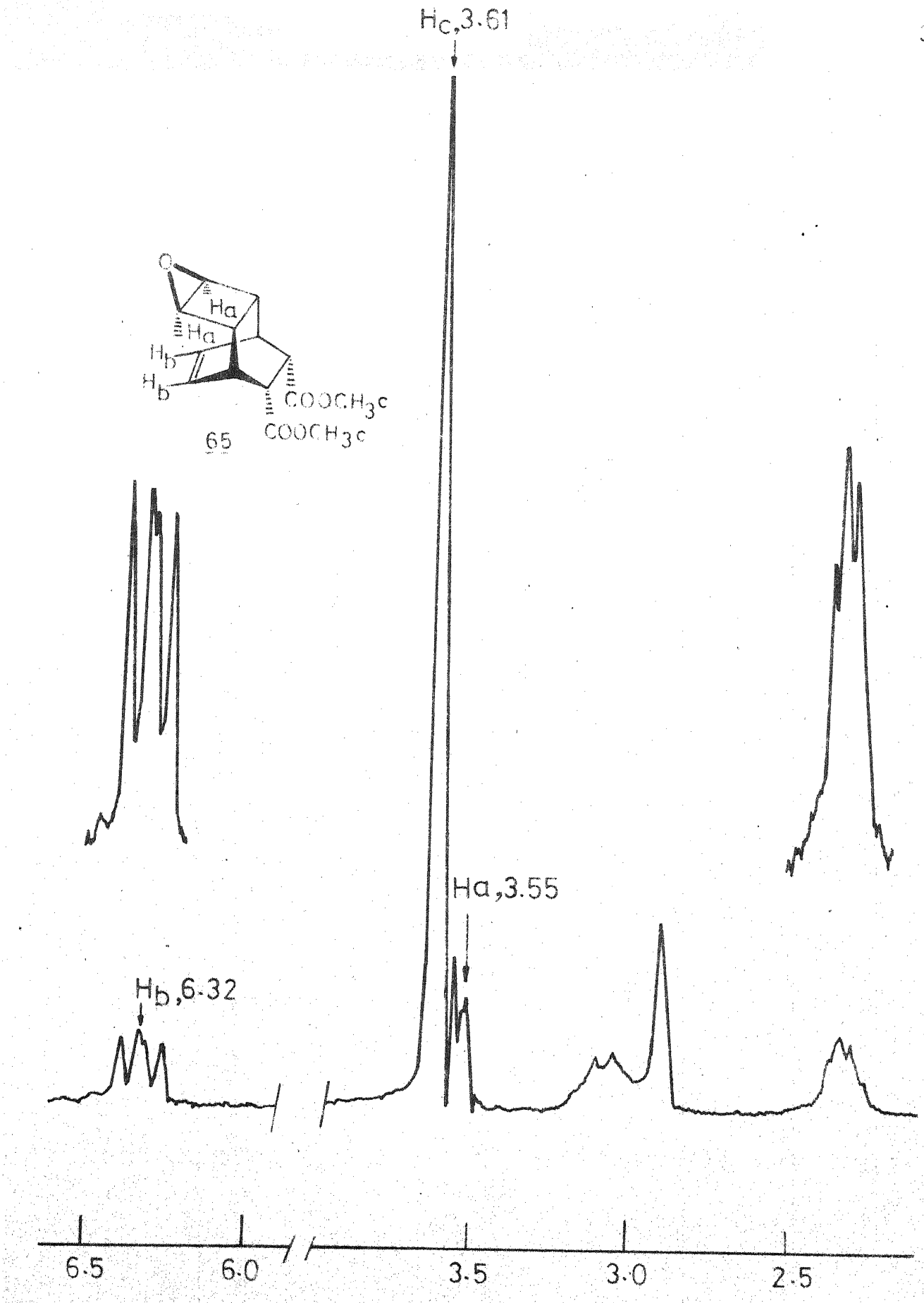
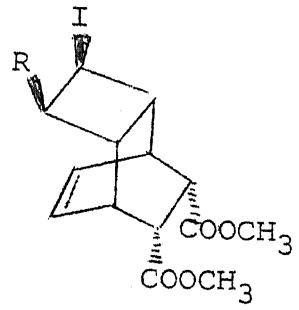
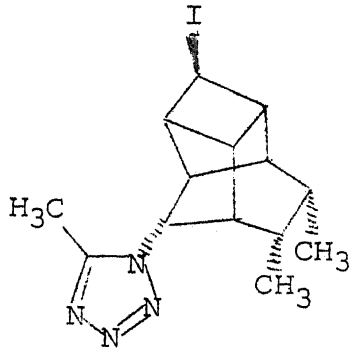


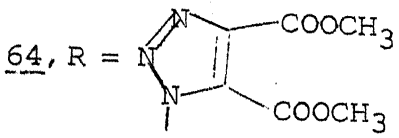
Fig. I.3 PMR spectrum (60 MHz) of 65



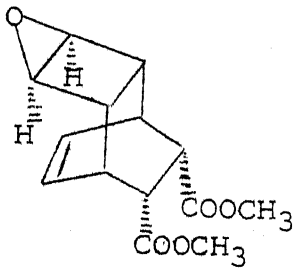
63, R = N_3



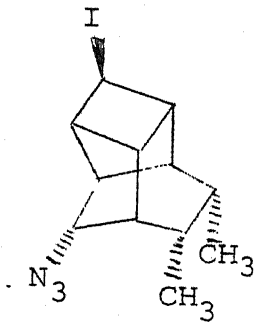
66



64, R =



65



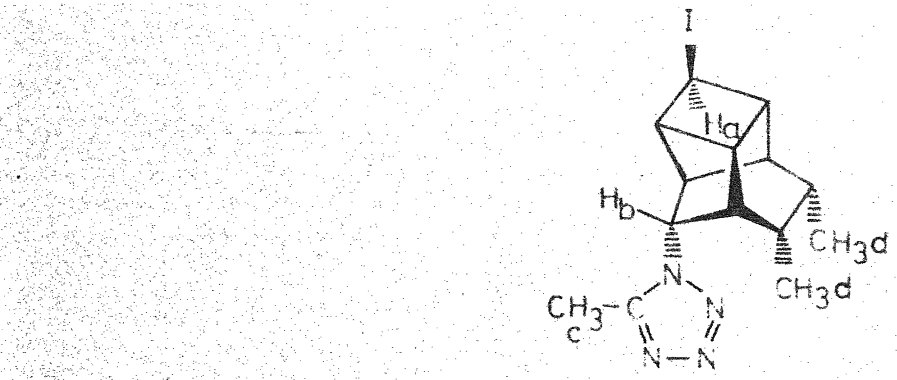
67

of a symmetrical triplet for the vinyl protons at C_7 and C_8 in tricyclo $[4.2.2.0^{2,5}]$ dec-7-enes is diagnostic of symmetrical endo substitution at C_3 and C_4 and has been used for the unambiguous assignment[67] of configuration at C_3 and C_4. The structure of the cis addition product has been further confirmed by its correlation with the oxymercuration product of 57 (vide infra).

Reaction of dimethyl compound (59) with iodine azide in acetonitrile gave a crystalline solid, mp 147-8° and

analysed for $C_{14}H_{19}N_4I$ indicating the participation of solvent in a Ritter-like reaction.[72] This product has been assigned the tetracyclic tetrazole structure (66) on the basis of spectral data. The pmr spectrum (Fig. I.4) showed two singlets at δ 4.55 and 3.93 due to methine protons attached to a tetrazolyl and iodo group along with a singlet at δ 2.6 due to a tetrazolyl methyl group. The spectrum was transparent in the olefinic proton region and suggested transannular participation by the C_7-C_8 double bond.[73] The formation of 66 *via* cross-type cyclization[74] is supported by the clean singlet resonances due to C_4 and C_7 protons (expected on the basis of vicinal dihedral angles) and is in agreement with the previously assigned structure of the cyclization products[74] of this system. When the addition of iodine azide to the diene (59) was repeated in methylene chloride medium, an unstable azido iodide (67) was obtained in high yield as the exclusive product and is assigned structure 67 on the basis of its ir spectrum (2110 cm^{-1}, azide) and pmr spectrum (Fig. I.5 , δ 4.16 & 3.75 singlets due to H-C-N_3 and H-C-I) which is analogous to 66. The azido iodide (67) was also found to be formed, although in small quantity, along with the tetrazole (66) in acetonitrile solvent.

Similarly, the addition of iodine azide to the ether (58) in acetonitrile furnished the tetrazole (68), mp 152-3°, as the major product and in methylene chloride the unstable tetracyclic azido iodide (69) was obtained. The structure



66

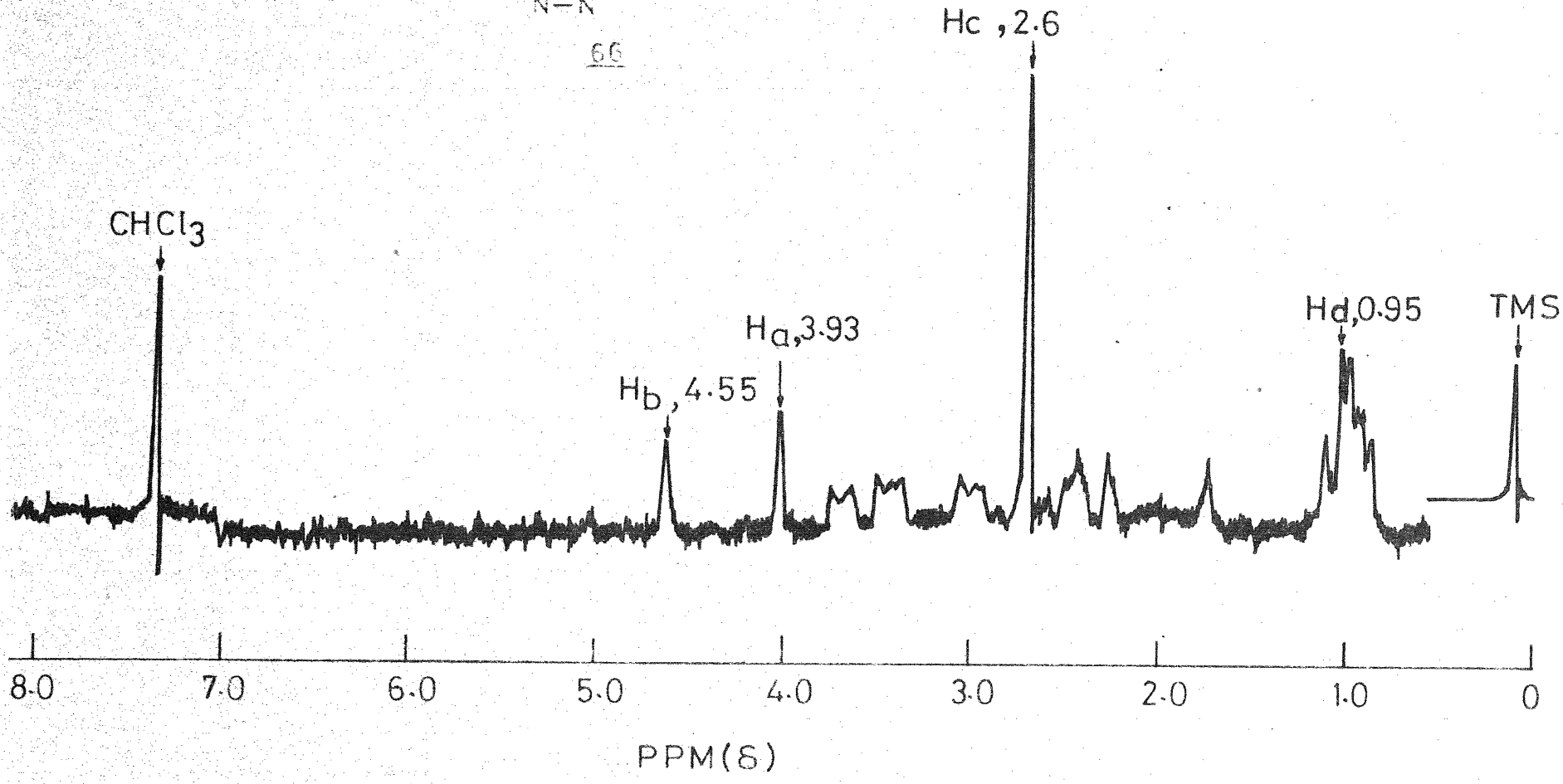
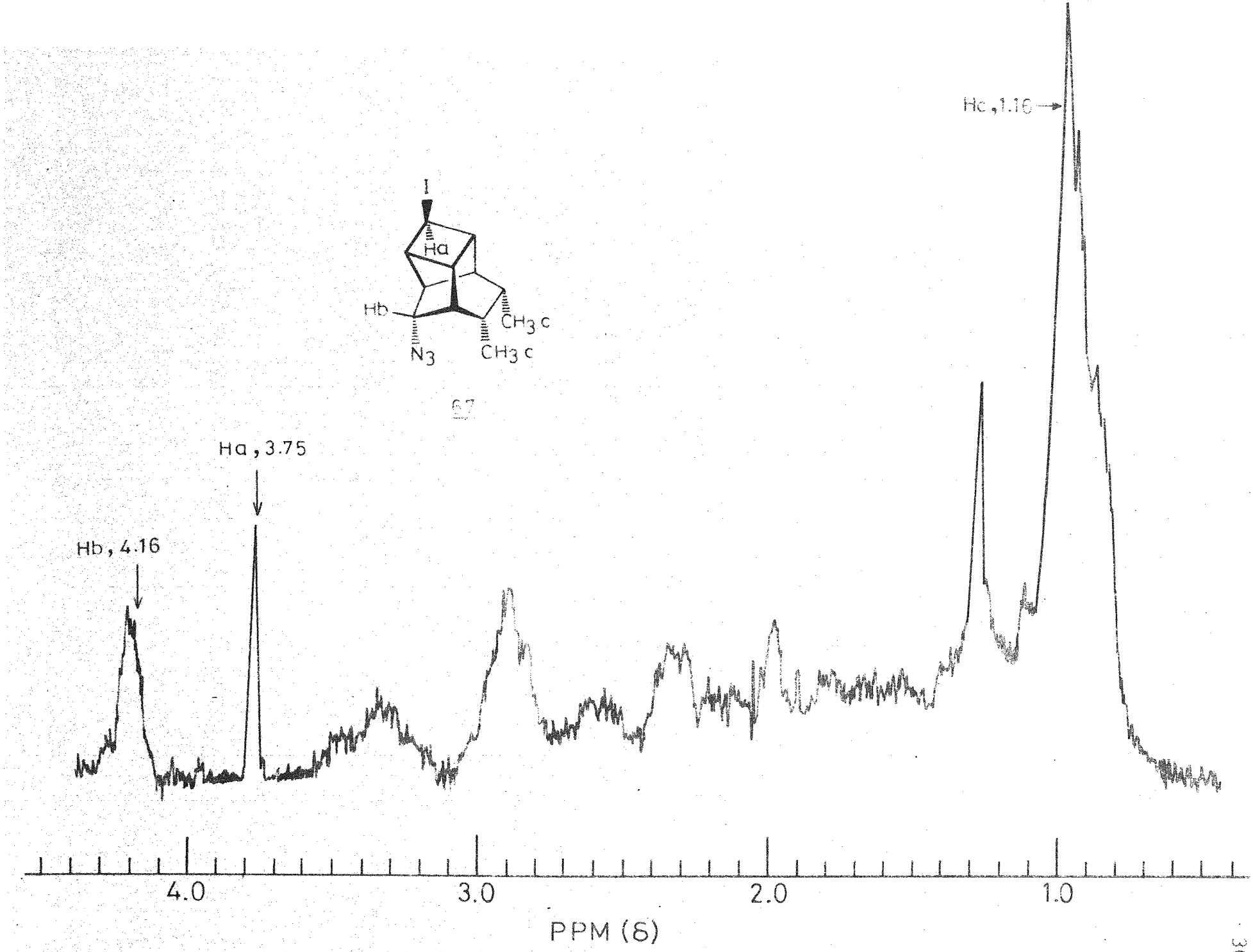


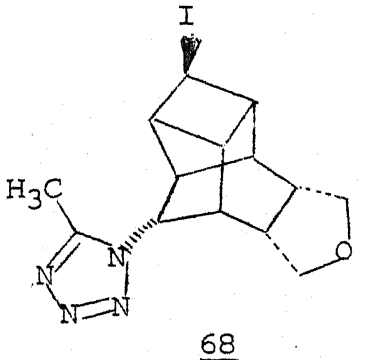
Fig. I.4 PMR spectrum (60MHz) of 66



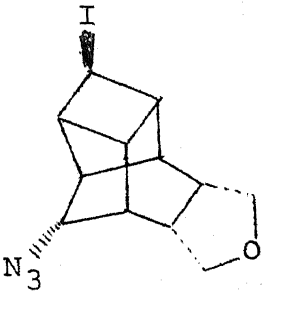
67

Fig. 1.5 PMR spectrum (60 MHz) of 67

of the tetrazole (68) follows from its pmr spectrum which exhibited singlets at δ 4.78 & 4.0 due to methine protons attached to a tetrazolyl and iodo group along with a singlet at δ 2.5 due to a tetrazolyl methyl group. A multiplet between δ 3.4-4.0 was assigned to the α-protons of the tetrahydrofuran moiety in 68. The azido iodide (69) was transparent in the olefinic proton region but displayed a doublet at δ 4.9 (J = 2 Hz) due to H-C-N_3 type grouping and a 5H multiplet between δ 3.4-4.1 due to the methine proton attached to the iodo group and the α-protons of the tetrahydrofuran ring. The ir spectrum of 69 had the characteristic azide absorption at 2120 cm^{-1}.



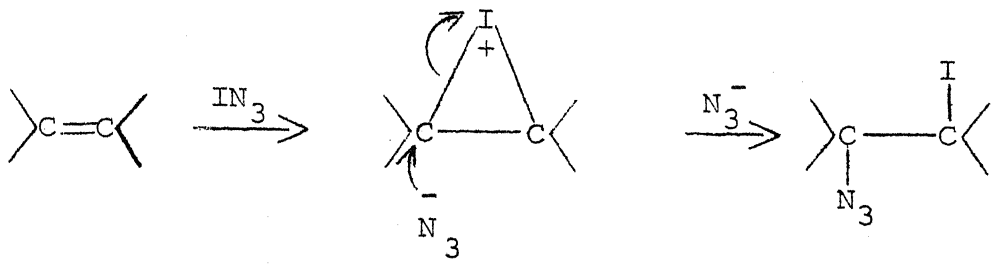
68



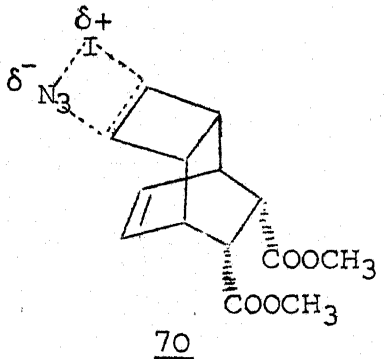
69

The addition of iodine azide to olefins has been shown by Hassner[9] to be a highly regio- and stereospecific process. The reaction proceeds via the electrophilic attack of IN_3 on the olefin with the formation of a three-membered-ring iodonium ion intermediate and preferential back side opening resulting in the trans-addition of the reagent (Scheme I.18). Numerous examples of such trans additions are recorded in the literature.[9]

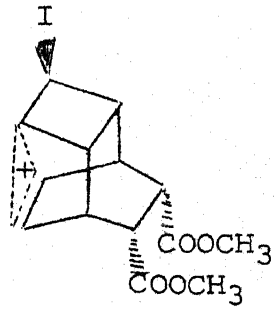
Scheme I.18



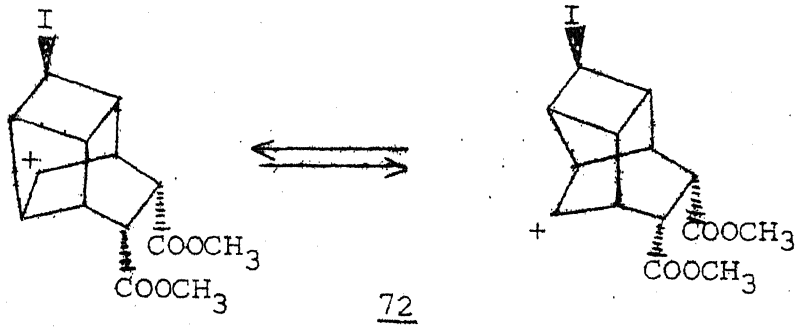
The formation of cis addition product 63 from diester (57) appears to be the first example of a cis addition of IN_3 to an olefin. Several mechanistic alternatives can be considered to account for this stereospecific cis addition. These may include a concerted four centred collapse via transition state (70), shielding of the endo face through intervention of either a bridged ion (71) or a pair of rapidly equilibrating classical ions (72) and dominance of twist strain factors as proposed by Traylor.[5] The four centred cis addition of IN_3 has been considered[9] by Hassner and rejected on the grounds that it is symmetry forbidden[51] and the large radius of iodine precludes a cis collapse. Also, complete variation in product formation in going from 57 to 59 without any



70

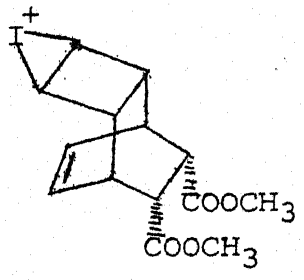


71

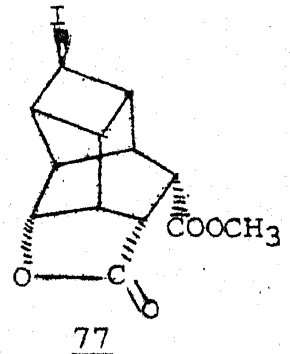


72

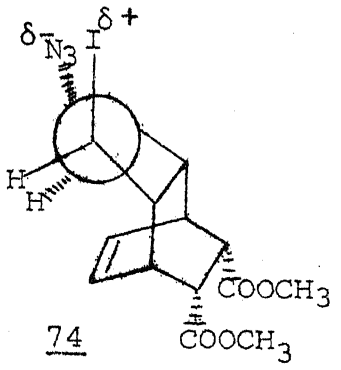
apparent change in the geometry of the olefinic moieties is not compatible with this mechanism. Therefore, we do not see any compelling reason to invoke this four centred polarized molecular addition in the present case. The intervention of 71 or 72 is discounted on the grounds that the presence of electron withdrawing carbomethoxy substituents at C_9 and C_{10} markedly decreases the availability of electrons from the participating C_7-C_8 double bond and should force more of the reaction of 57 through the iodonium ion (73). This contention is supported by the fact that in the IN_3 addition to dimethyl compound (59) and ether (58), where facile π participation and formation of ions related to 71 and 72 is possible, only cyclised tetracyclic products are formed and no



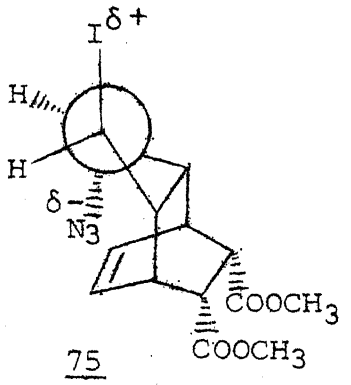
73



77



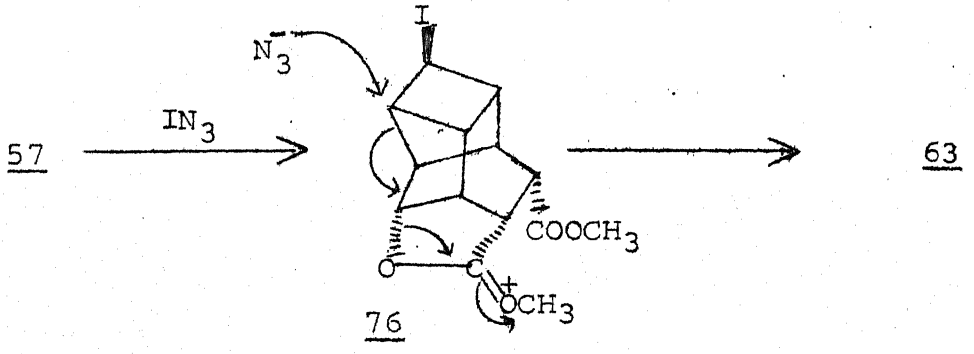
74



75

cis addition product has been encountered. We, therefore, believe that the formation of cis addition product 63 is best rationalized on the basis of twist strain theory[5] and the cis transition state (74) is favoured over the trans coplanar transition state (75). Lastly, there exists an interesting possibility that cis addition of IN_3 to 57 may arise via an intermediate (76) formed through the carbomethoxy participation (Scheme I.19). Azide ion assisted opening of 76 (see arrows) might lead to 63. However, the iodo lactone (77)

Scheme I.19



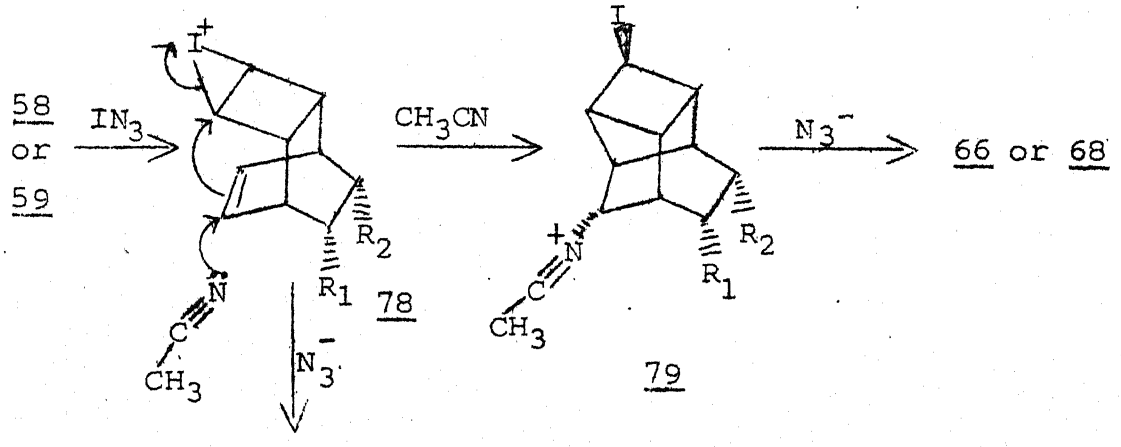
76

related to the intermediate 76 is recovered unchanged when subjected to either the reaction conditions of iodine azide addition (ICl and sodium azide in acetonitrile at -5°) or

more stringent conditions (sodium azide in refluxing aq. acetonitrile) for prolonged period of time.

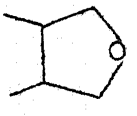
The formation of the tetrazoles (66) and (68) from 59 and 58 respectively represent interesting examples of transannular Hassner-Ritter reaction. Their formation is rationalised on the basis of the solvent assisted opening of the initially formed iodinium ion (78) to give the Ritter reaction intermediate (79), which undergoes cycloaddition with azide ion to form the substituted tetrazoles. When the reaction is carried out in CH_2Cl_2 only the azido iodide results via the participation and nucleophilic capture by the azide ion (Scheme I.20).

Scheme I.20



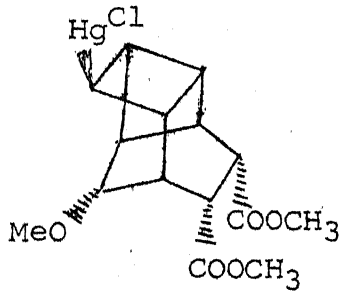
$R_1 = R_2 = CH_3$

R_1 & R_2 =

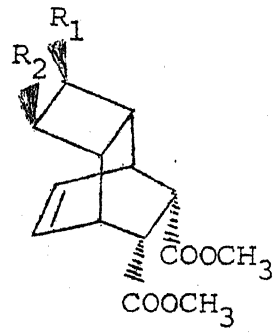


Mercuric Acetate Additions

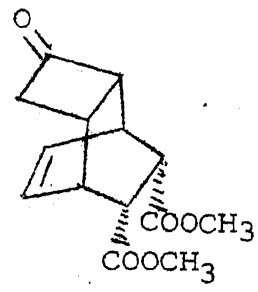
Methoxymercuration of diester (57) has been investigated by Cookson et al.,[75] resulting in the formation of a solid, mp 190-92°, to which they assigned the tetracyclic structure 80. Repetition* of this methoxymercuration in our



80



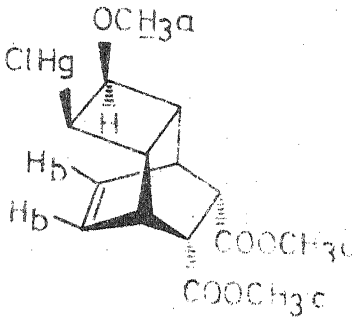
81, R_1=OMe, R_2=HgCl
82, R_1=OH, R_2= HgCl
83, R_1=OH, R_2= H



84

hands led to the formation of a crystalline organomercurial, mp 193-5°, whose pmr spectrum (Fig. I.6) exhibited a 2H olefinic proton triplet at δ 6.7, a 3H methoxyl singlet at δ 3.23 and a multiplet due to a proton attached to the methoxy group at δ 3.60 along with other resonances compatible with structure 81. Similarly, hydroxymercuration of 57 furnished the addition product 82, mp 164-5°, and displayed in its pmr spectrum 2H olefinic proton signal at δ 6.71 indicating addition to one of the double bonds of 57. Regiospecific addition to the cyclobutene ring was established via hydroxymercuration-demercuration of 57 to 83 and oxidation with CrO_3-pyridine

*Recently, methoxymercuration of diester (57) has been reported in literature.[76]



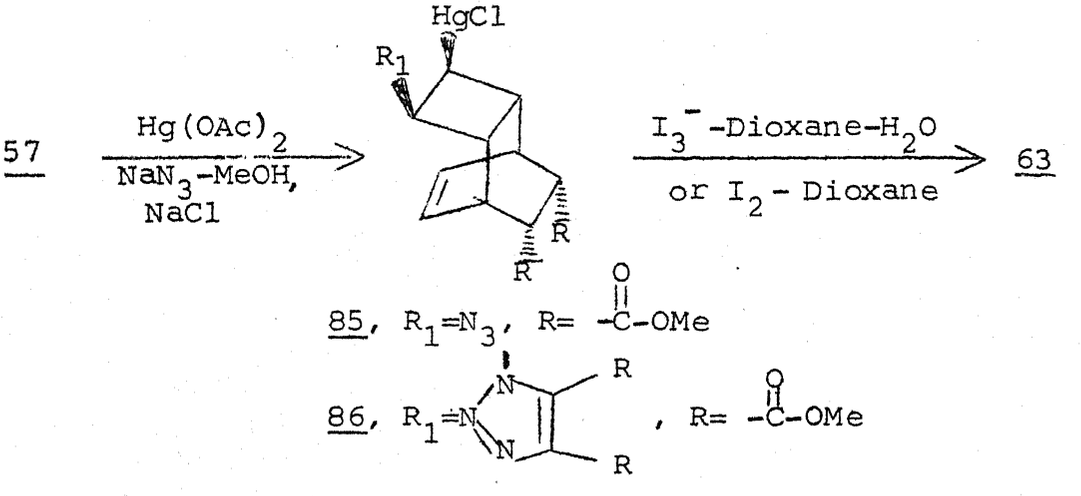
81

Fig. I.6 PMR spectrum (60MHz) of 81

reagent to the known[77] cyclobutanone (84).

The cis stereochemistry of the oxymercuration products 81 and 82 was demonstrated on the basis of pmr data[67] and chemical correlation with the IN_3 adduct (63) as shown in Scheme I.21. Reaction of 57 with $Hg(OAc)_2$ in methanol in the presence of azide ion furnished the azido mercurial 85, mp 155-57°. The azido mercurial (85) as well as its dipolar addition product 86 with dimethyl acetylenedicarboxylate showed clean triplet signals for the C_7-C_8 olefinic protons. Iodination of 85 with I_2 or triiodide ion in dioxane gave a

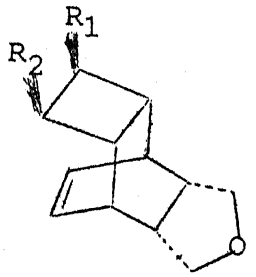
Scheme I.21



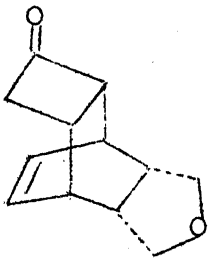
crystalline product identical in all respects with 63. The iodination of organomercurials with triiodide ion in polar medium has been shown[78] to proceed with retention of configuration.

Methoxymercuration of ether (58) and dimethyl compound (59) proceeded rapidly and smoothly to furnish the cis-

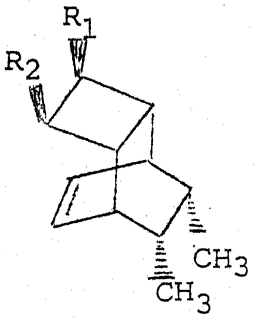
methoxy mercurials (87) and (88) which showed olefinic triplets at δ 6.56 & 6.53 respectively (Fig. I.7 & I.8). The selective addition to the cyclobutene double bond in each case was established *via* a reaction sequence involving hydroxymercuration to 89 & 90, demercuration with $NaBH_4$ to 91 & 92



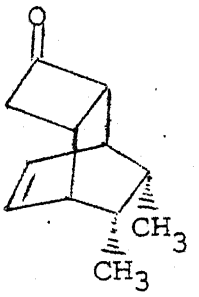
87, R_1 = OMe, R_2 = HgCl
89, R_1 = OH, R_2 = HgCl
91, R_1 = OH, R_2 = H



93



88, R_1 = OMe, R_2 = HgCl
90, R_1 = OH, R_2 = HgCl
92, R_1 = OH, R_2 = H



94

and chromium trioxide-pyridine oxidation to cyclobutanones (93) & (94) respectively. The rate of methoxy- and hydroxymercuration of the dienes greatly increased (vide experimental)

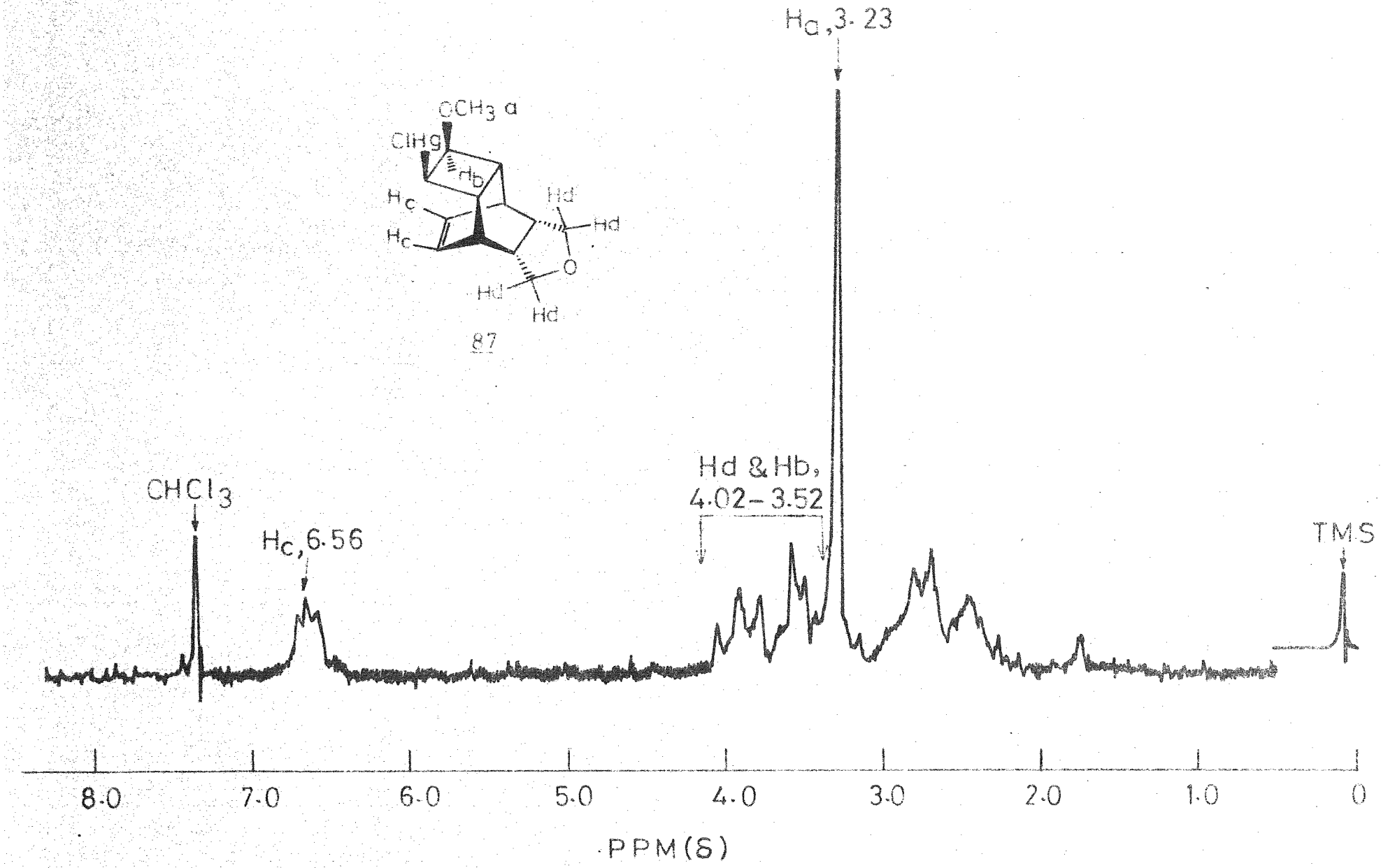


Fig. I.7 PMR spectrum (60 MHz) of 87

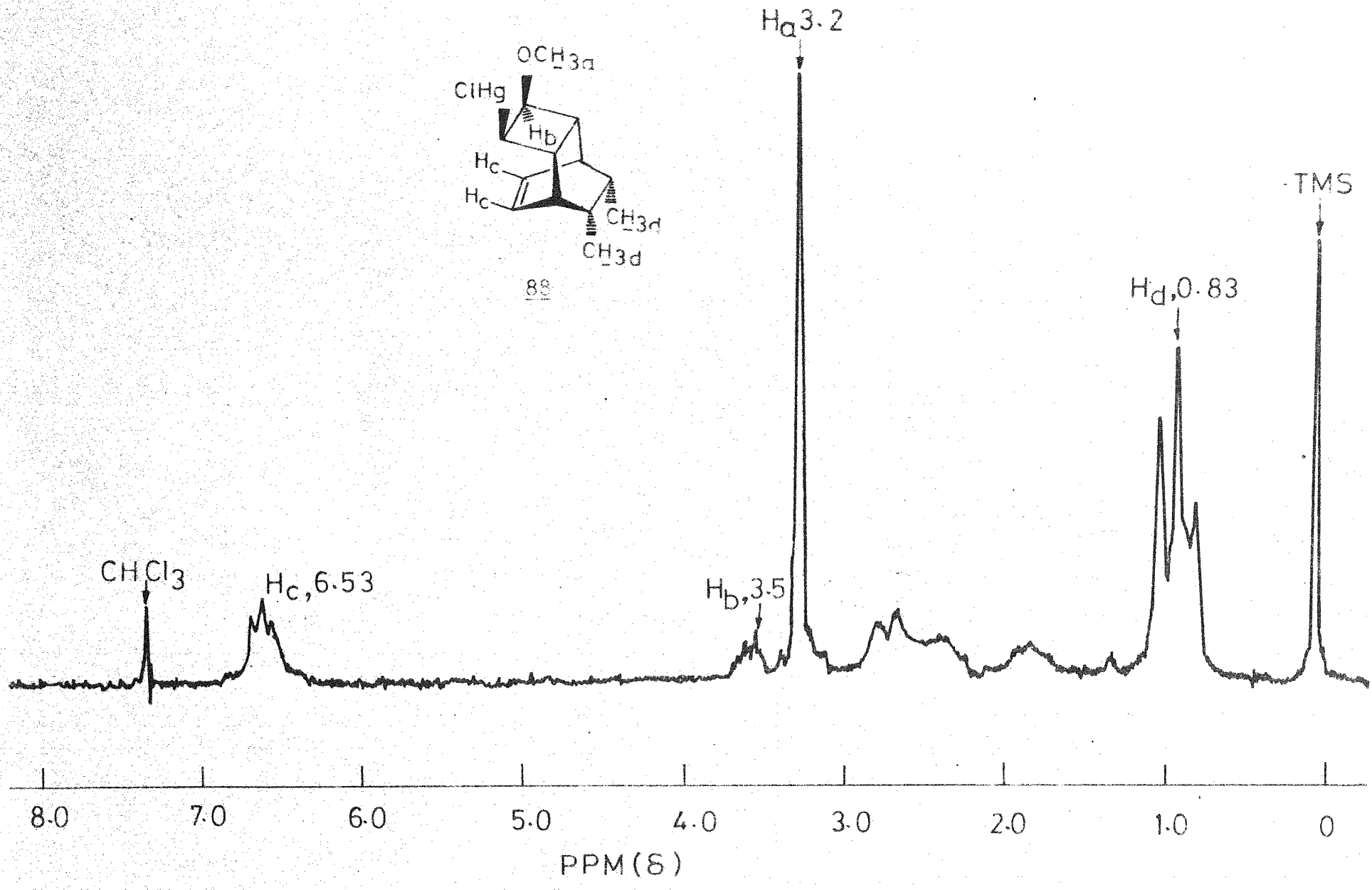
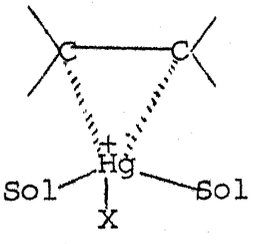


Fig. I.8 PMR spectrum (60 MHz) of 88

in going from 57 to 58 and 59 indicating a strong transannular enhancement in the reactivity of the cyclobutene ring as a result of variation in substituents (electron withdrawing ester to electron donating methyl group) at C_9 and C_{10}. Similar observation was also made in the case of IN_3 addition (vide experimental).

The oxymercuration of simple olefins is known to be a stereospecific trans-addition.[11,12] On the other hand, addition of mercuric salts to strained olefins like norbornene[5,15] and bicyclo[2.1.1]hexene[22] (16) has been shown to be a stereospecific cis addition. Several mechanistic schemes based on molecular addition, twist strain theory, torsional effects, formation of equilibrating classical ions and nonclassical participation have been proffered to explain the formation of cis,exo products, particularly in case of norbornene 8.[5] Among these, the last three explanations have been eliminated on the grounds that the factors controlling the stereochemistry of addition in strained olefins are not related to those governing the exo:endo rate ratios in norbornyl solvolysis. Recently, Bach and Richter[39] have studied in detail the oxymercuration of bicyclo[2.2.2]oct-2-ene (17) and explain the formation of both cis and trans-addition products via a common solvated mercurinium ion intermediate (95). It has been suggested by them that cis-oxymercurials may arise via the attack of displaced ligand (X^-) on 95 before the solvent separation and the trans-oxymercurials result via usual back

side displacement. In the present case, oxymercuration of dienes, 57, 58 & 59 with $Hg(OAc)_2$ in methanolic and aqueous medium proceeds without the formation of any detectable amounts of acetoxymercuration product and thus rules out a molecular mechanism involving the collapse of the acetate ligand on mercury in the intermediate 96 to furnish the cis-products. The exclusive formation of cis products in



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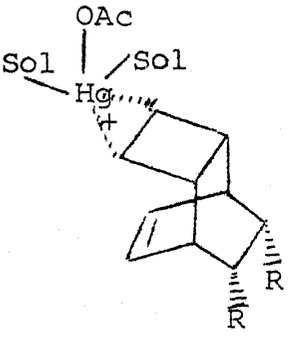

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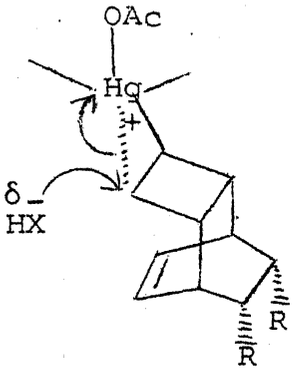

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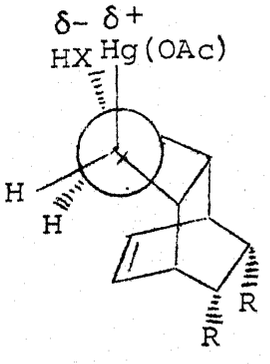

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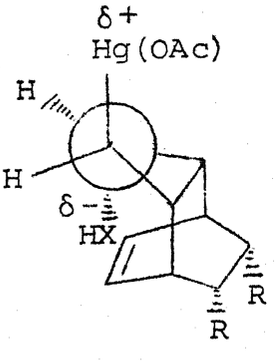


98

oxymercuration of 57, 58 & 59, consistent absence of products arising out of either carbonium ion rearrangement or trans-annular participation is best rationalised in terms of the twist strain theory.[5] The cis-transition state (97) is

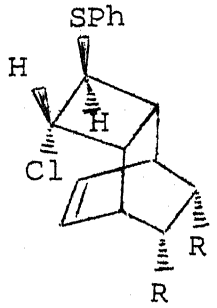
favoured over the strained trans-coplanar transition state (98). It is conceivable that the bond opposition inherent in the transition state for cis-addition can be minimised via the conversion of 97 to an unsymmetrical ion (99). This can be expected in view of the relatively long carbon-mercury bond distance in the π-complex of $\sim$2.3 Å.[2]

The oxymercuration of dienes 57, 58 and 59 represents the first example of cis-addition to a cyclobutene. The cyclobutene itself has been shown to furnish exclusively trans products on oxymercuration.[40,62] It is quite surprising that no transannular participation is observed during oxymercuration of our system in marked contrast to the behaviour of 1,5-cyclooctadiene,[79] Dewar benzene,[80] norbornadiene[20] and 9,10-benzotricyclo[4.2.2.$2^{2,5}$]dodeca-3,7,9-triene.[81]

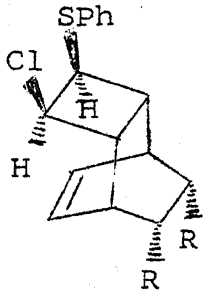
Benzenesulphenyl Chloride Additions

Addition of benzenesulphenyl chloride (PhSCl) to a methylene chloride solution (-20°) of diester (57) containing small amount of suspended calcium carbonate furnished a 3:1 mixture of two adducts in near quantitative yield. The major and the minor adducts were readily separated by column chromatography on silica gel and were assigned the trans-100 and cis-101 structures respectively on the basis of pmr spectral analysis (Fig. I.9 and I.10). The trans-adduct 100, mp 119-20°, displayed a diffused multiplet centred at δ 6.46

due to C_7 and C_8 olefinic protons indicating unsymmetrical endo substitution at C_3 and C_4 (Fig. I.9). Furthermore,



100, R = $COOCH_3$
104, R = CH_3



101, R = $COOCH_3$
105, R = CH_3

the exo proton (δ 4.42) at C_3 in trans adduct 100 exhibited significant shielding due to the cis-vicinal phenylthio group as compared to the C_3 endo proton (δ 4.9) in the cis-adduct 101. Examples of shielding of cis-vicinal protons by the phenylthio group have been previously recorded in literature.[37] The cis-adduct (101), mp 201-3°, on the other hand, showed its olefinic protons as a triplet at δ 6.55 due to symmetrical endo substitution at C_3 and C_4 along with other expected resonances (Fig. I.10).

Similarly, addition of PhSCl to tetracyclic ether 58 furnished a 3:1 mixture of trans-adduct 102, mp 143-4° and cis adduct 103, mp 152-3°. Structures to the trans and cis adducts were once again deduced from the multiplicity of the olefinic proton signal and the relative shielding of the C_3 exo proton (δ 4.5) in the trans adduct 102 (Fig. I.11) as compared to C_3 endo proton (δ 4.8) in the cis adduct 103.

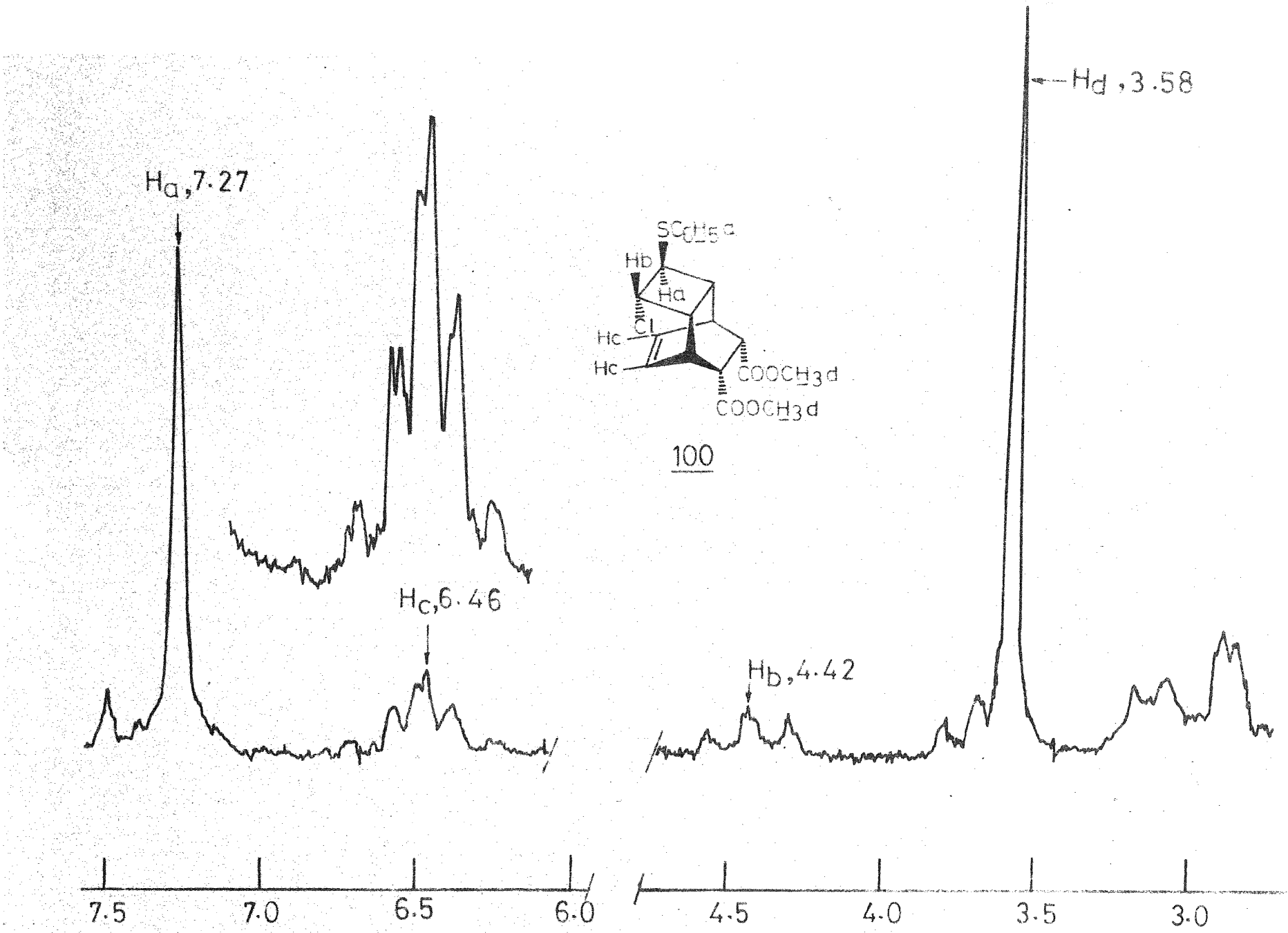


Fig. I.9 PMR spectrum (60 MHz) of 100

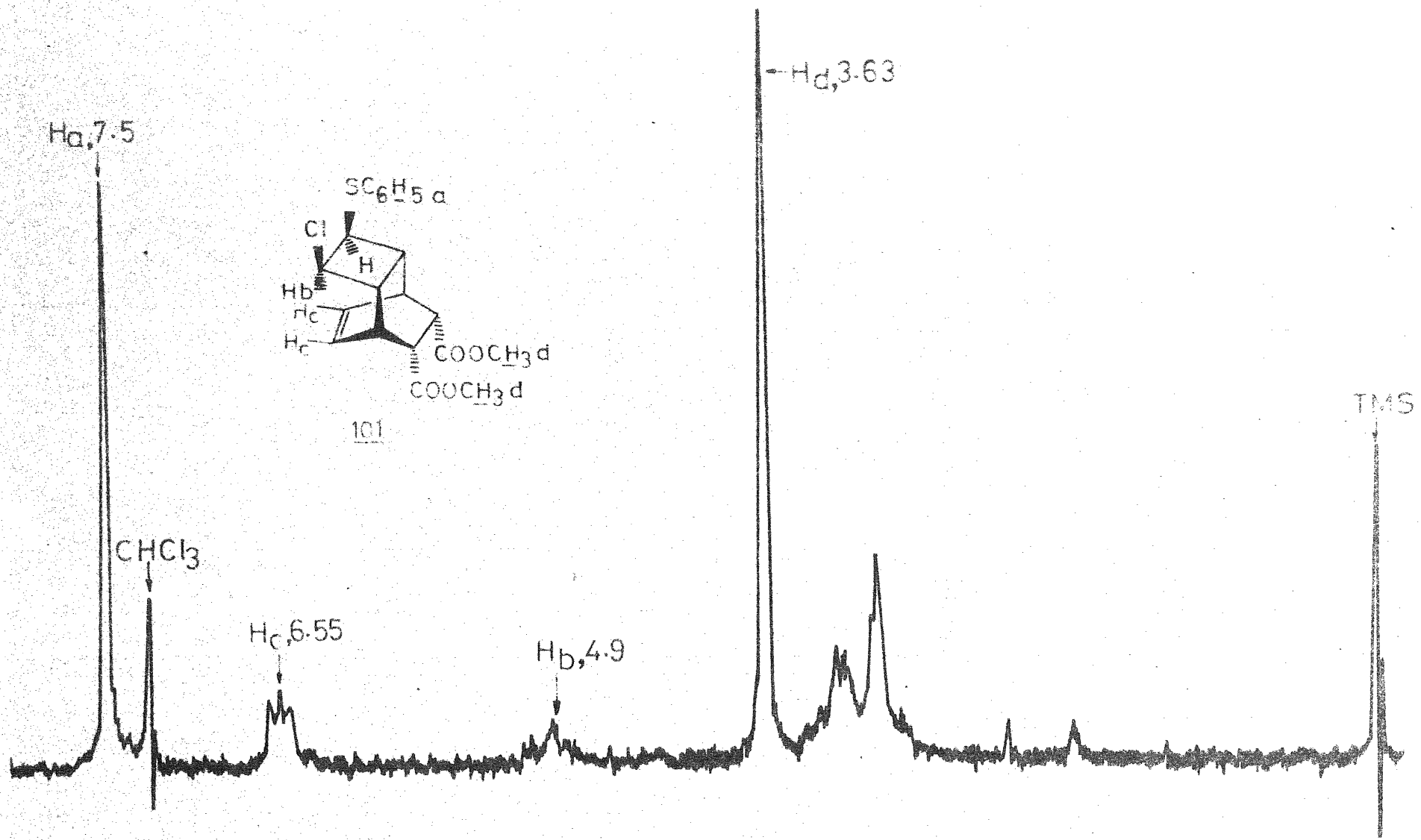


Fig. I.10 PMR spectrum (60 MHz) of 101

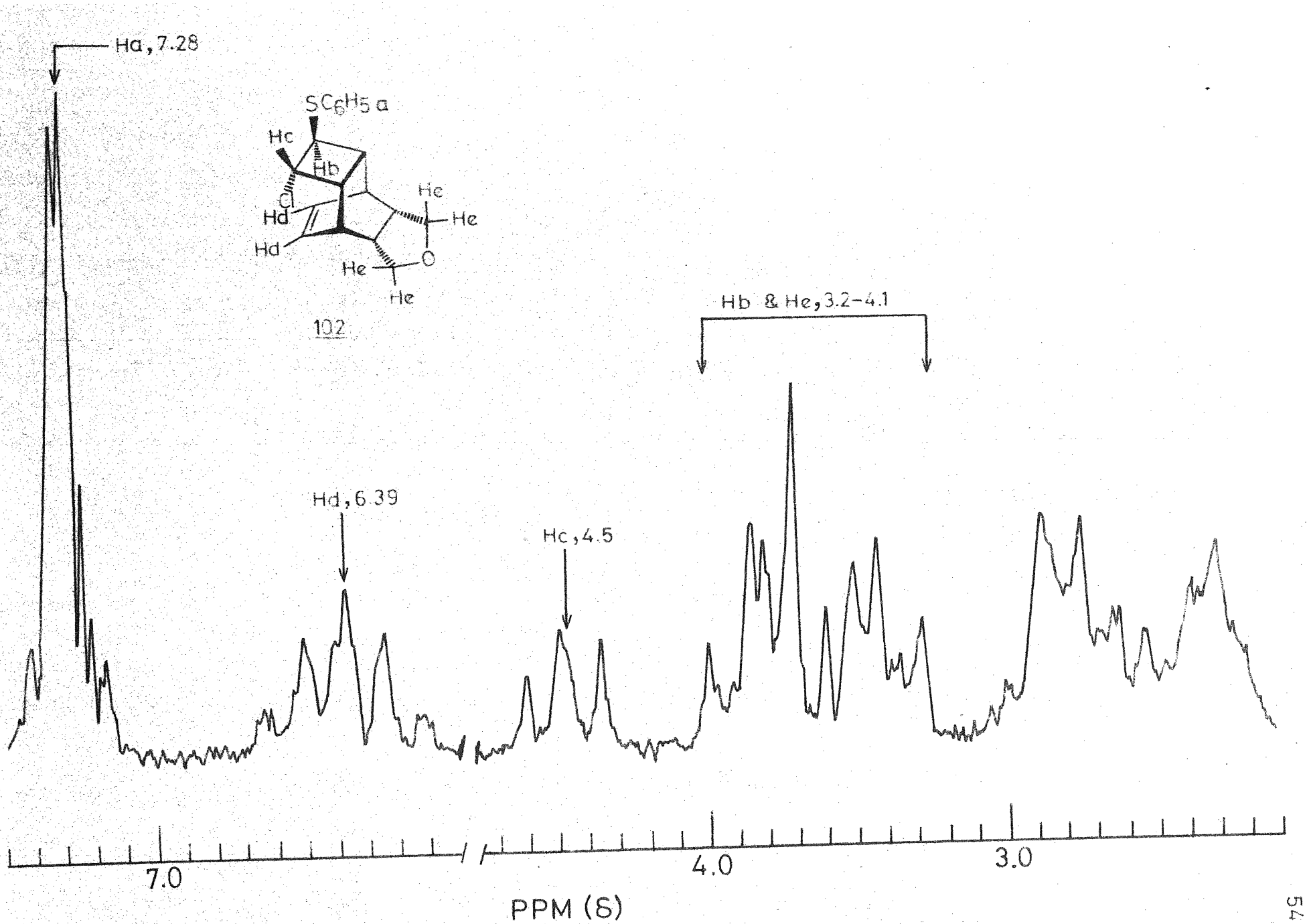


Fig. I.11 PMR spectrum (60 MHz) of 102

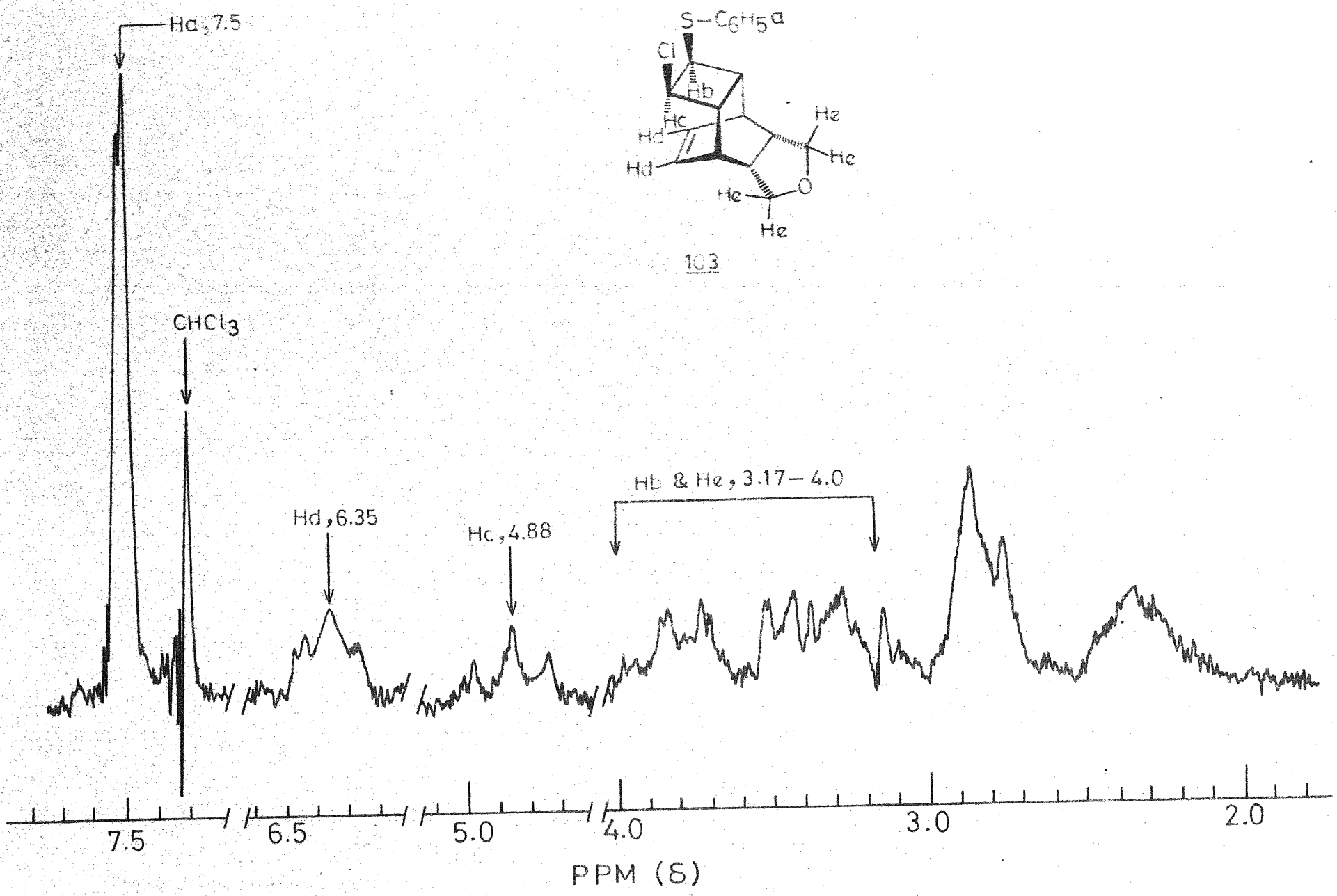


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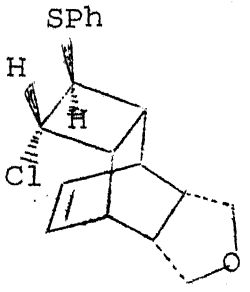
Fig. 1.12 PMR spectrum (60 MHz) of 103



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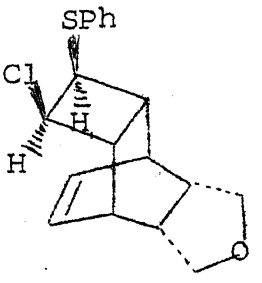


103

(Fig. I.12). Likewise, addition of PhSCl to the dimethyl compound 59 also gave a mixture of trans-104 and cis-105 addition products. However, in this case only the trans-adduct 104, mp 86°, could be obtained pure and characterised on the basis of pmr spectrum (Fig. I.13). The presence of the cis-adduct 105 was only inferred indirectly by tlc and spectral behaviour of the mixture of two adducts.

Finally, it was shown that cis and trans-addition products 100-103 formed from dienes 57 & 58 were stable under the reaction conditions. This observation clearly established that the mixture of cis and trans adducts was not formed due to the involvement of any isomerisation or equilibrium process during the reaction.

Addition of sulphenyl halides to olefins have been extensively studied[10] and are considered to be highly stereospecific trans-additions proceeding in two steps via episulphonium (thiiranium)ion intermediate 106 (Scheme I.22).

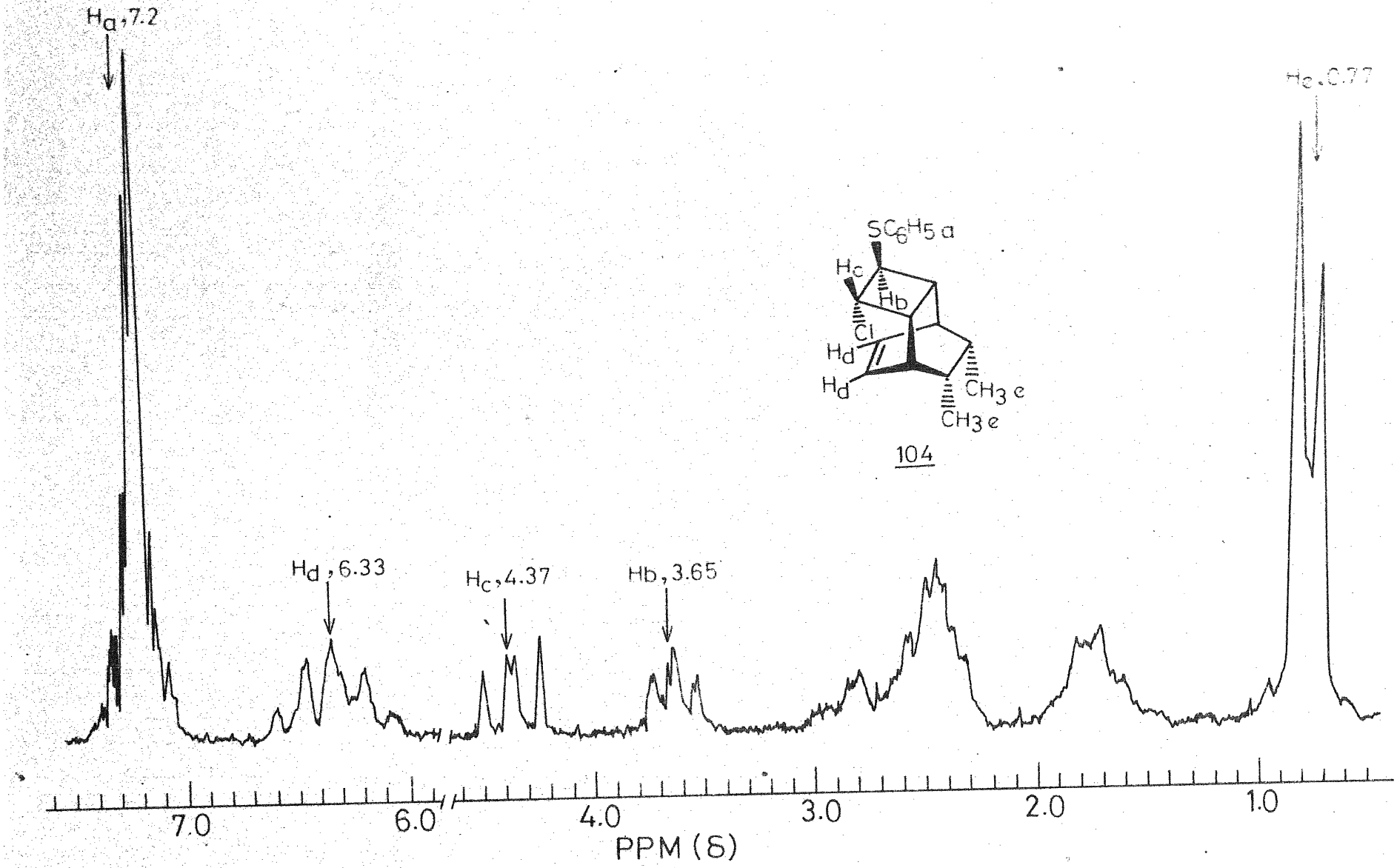
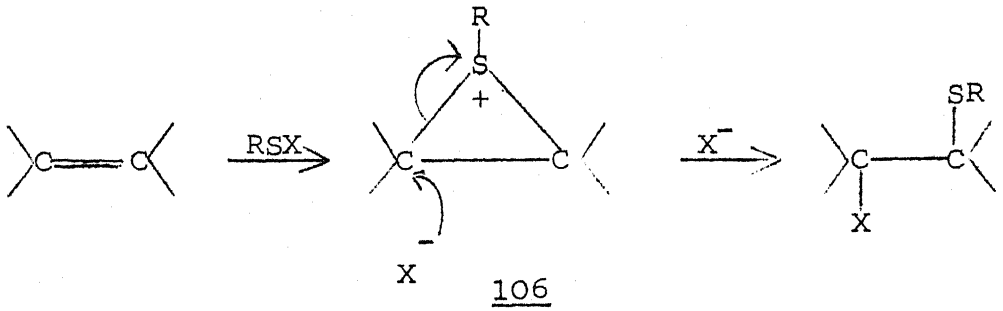


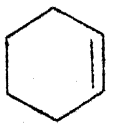
Fig. I.13 PMR spectrum (60 MHz) of 104

Scheme I.22



106

Simple olefins like cyclohexene[10] (107) as well as strained olefins e.g., norbornene[46] (8), bicyclo[2.1.1]hex-2-ene[22] (16) and acenaphthene[82] (108), with marked propensity for cis-



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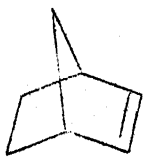

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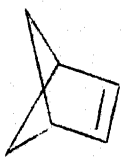

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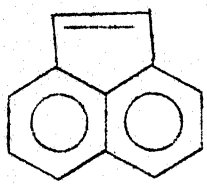

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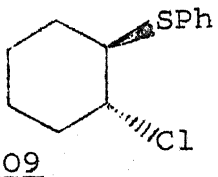

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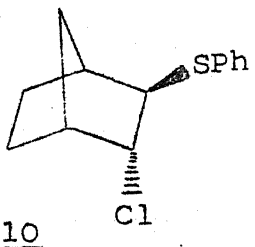

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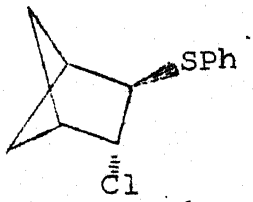

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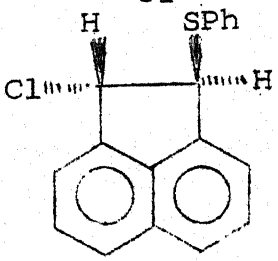
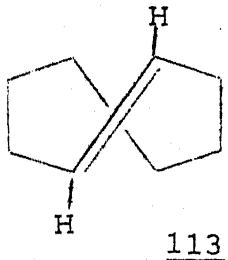


112

additions conform to the above mechanism and furnish exclusive trans-products 109-112 with benzenesulphenyl chloride. Recently, stable solutions of episulphonium ion salts have been prepared at low temperature and shown to react stereospecifically with nucleophiles to furnish trans-products.[83] In case of olefins like trans-cyclooctene 113, where only one face of the π bond is exposed, an unusual reaction occurs[84] leading to the formation of allylic sulphide 114. Although, some recent reports have questioned[85,86] the involvement of



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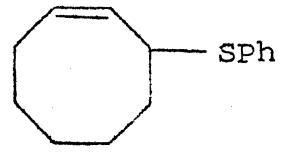
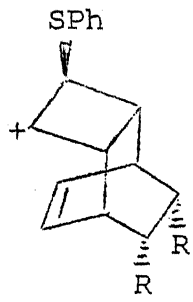


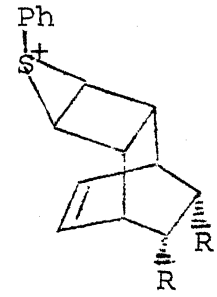
114

episulphonium ions in the PhSCl addition to olefins, the rule of trans-addition has not been violated.

The results of PhSCl addition reported here appear to be the first example of nonstereospecific addition of this reagent to an olefin. The formation of both cis- and trans-addition products from 57, 58 and 59 with benzenesulphenyl chloride can be explained through a free carbonium ion intermediate 115 but is not compatible with the intermediacy of episulphonium ion (116) in the product determining step of the reaction. This contention is supported by the results of addition of iodine azide and mercuric acetate (vide supra),



115



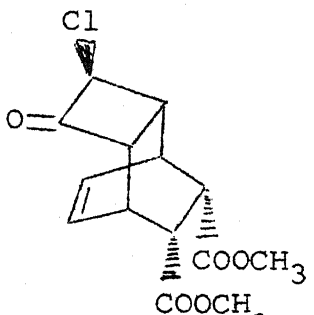
116

which proceed via the corresponding three membered 'onium' ion intermediates and furnish exclusive cis products under the dominant influence of twist strain factors. We believe that the initially formed episulphonium ion intermediate(115) with a thiabicyclo[2.1.0]pentane moiety is quite strained as compared to the corresponding iodonium 73 and mercurinium ions 99 (cf. the shorter C-S bond distance ~ 1.7-1.8 Å vs C-I ~2.2 Å and C-Hg ~2.3 Å bond distances[2,87]), and is likely to exist as the free carbonium ion (115). This ion 115 undergoes preferential addition from the endo face leading to preponderance of trans-addition products 100, 102 and 104 as the exo face is hindered by the presence of phenylthio group. This type of steric hinderance to exo-addition by exo bulky groups has been previously observed[68] during radical additions to the tricyclo[4.2.2.$0^{2,5}$]deca-3,7-diene ring system (Scheme I.16).

Miscelleneous Additions

The addition of nitrosyl chloride generated in situ with diester (57) led to the formation of unrearranged

chloroketone (117) formed through the acid hydrolysis of the oxime and no 1:1 adduct was encountered. Hydroboration of 57 in acetic acid[88] proceeded smoothly to give the alcohol (83) identical with the oxymercuration-demercuration product of 57. Finally, the addition of chlorosulphonyl isocyanate (CSI) to 57 was investigated but to our surprise only the anhydride (60) was formed in this reaction in high yield.



117

Finally, the contrasting behaviour of dienes 57, 58 and 59 towards iodine azide, halogens,[74] iodine nitrate[74] etc (rearrangement) on one hand and of mercuric acetate, nitrosyl chloride, benzenesulphenyl chloride etc (no rearrangement) on the other seems to be governed by the nature of the electrophilic addend, its ability to stabilise the neighbouring charge and medium effects.

I.4 EXPERIMENTAL SECTION

Melting points and boiling points are uncorrected. Melting points were taken in capillaries on a Thomas-Hoover melting point apparatus. Boiling points refer to bath

temperature in those cases where short path bulb to bulb distillations were carried out. The petroleum ether corresponds to the fraction bp 60-80°. All solvent extracts were washed with brine and dried over anhydrous sodium sulphate. Infrared spectra were recorded on a Perkin-Elmer Model 137B spectrophotometer as neat liquids or solids as KBr discs. PMR spectra were obtained on approximately 10-15% solutions in CCl_4 or $CDCl_3$ on a Varian A-60 spectrometer. The chemical shifts are reported in parts per million downfield from internal tetramethylsilane at 0.00 as internal standard. The abbreviations s, d, t, q, m and en refer to singlet, doublet, triplet, quartet, multiplet and envelop respectively. Microanalyses were performed by Mr. A.H. Siddiqui in the Microanalytical Laboratory of our Department on Coleman automatic carbon-hydrogen and nitrogen analysers.

9,10-Dicarbomethoxytricyclo$\left[4.2.2.0^{2,5}\right]$deca-3,7-diene (57)

The diester (57) was prepared essentially according to literature procedure.[65] In a 100 ml RB flask, fitted with a condenser, cyclooctatetraene (10.4 g, 0.1 mol) and finely powdered maleic anhydride (10 g, 0.1 mol) were mixed and heated in an oil bath at 165-70° for 1 hr. The reaction product was cooled and directly sublimed at 150°/1 mm to give 17.5 g(85%) yield of COT-maleic anhydride adduct (60), mp 168° (lit.[65], 168°).

IR spectrum (KBr): 1845, 1780 (anhydride carbonyl), 1225, 1085 and 785 cm^{-1}.

The COT- maleic anhydride adduct (60, 10 g) in methanol (60 ml) was refluxed for 5 hr with catalytic amount of conc. H_2SO_4 (3 ml). The reaction mixture was cooled, poured into water (75 ml) and extracted with ether (50 ml x 3). The ethereal layer was washed with aq. sodium bicarbonate, water and dried. Removal of solvent yielded 10.8 g (86%) of diester (57), bp 130°/1.5 mm, mp 52-53° (lit.[65] 52°).

IR spectrum (KBr): 1745 and 1200 cm^{-1} (ester).

PMR spectrum (CCl_4): δ 5.75 - 5.95 (olefinic, 4H, m), 3.51 ($C\underline{H}_3$-O-$\dot{C}$=O, 6H, s) and 2.65-2.95 (C-$\underline{H}$ ring, 6H, m).

Tetracyclic ether[70] (58)

The above diester (57, 5 g) in dry tetrahydrofuran (THF, 50 ml) was reduced with $LiAlH_4$ (2.3 g) for 8 hr at reflux temp. Decomposition with moist ether and dil. H_2SO_4 and usual work-up furnished a diol (61) as glistening stout needles, mp 115° (lit.[70] 117°).

IR spectrum (KBr): 3300, 1040 cm^{-1} (hydroxyl).

PMR spectrum ($CDCl_3$): δ 5.76 (olefinic, 4H, m), 4.2 ($\underline{H}$-O-, 2H, s), 3.56 (-$\underline{CH_2}$-OH, 4H, m) and 2-2.8 (C-$\underline{H}$ ring, 6H, en).

In a 250 ml RB flask fitted with a Dean-Stark apparatus, diol (61, 4.0 g) in dry benzene (50 ml) containing p-toluenesulphonic acid (100 mg) was placed and the mixture refluxed for nearly 6 hr. The reaction mixture was poured

into aq. sodium bicarbonate and the benzene layer was separated. The organic phase was washed, dried, stripped of solvent and distilled to give 3 g of 58 as a colourless mobile liquid, bp 88-90°/3 mm; mp 38°.

IR spectrum (neat): 1110 cm^{-1} (ether).

PMR spectrum (CCl_4): δ 5.83 (olefinic, 4H, m), 3.5 ($-\underline{CH_2}-O-\underline{CH_2}-$, 4H, pair of q) and 2.17-2.73 (C-H ring, 6H, en).

9,10-Dimethyltricyclo[4.2.2.$0^{2,5}$]deca-3,7-diene (59)

The diol (61, 4.0 g) in dry pyridine (25 ml) was allowed to react with an excess of methanesulphonyl chloride (7 ml) and the reaction mixture kept in a refrigerator for 12 hr. The reaction mixture was poured into ice water and extracted with CH_2Cl_2 (50 ml x 2). The CH_2Cl_2 extract was washed successively with dil. HCl (50 ml x 3), sodium bicarbonate (50 ml x 2) and brine. Drying and removal of solvent gave (5.3 g) of the dimesylate (62), mp 136-7°.

IR spectrum (KBr): 1330, 1155 cm^{-1} (sulphonate).

Anal. for $C_{14}H_{20}O_6S_2$ Calcd: C, 48.25; H, 5.79.
Found: C, 48.85; H, 5.68.

To a stirred slurry of $LiAlH_4$ (2.5 g) in dry THF (50 ml), a solution of the dimesylate (62, 5 g in 35 ml of THF) was added dropwise and the mixture was refluxed for 8 hr. The reaction mixture was quenched by the careful addition of moist ether followed by 25 ml of 10% dil. H_2SO_4. The organic

material was extracted with pet ether (25 ml x 3), washed and dried. Removal of solvent and distillation gave 2.1 g of a colourless oil, bp 100-102° (bath, 11 mm).

IR spectrum (neat): 3140 (olefinic), 1640, 788, 770, 745 and 710 cm^{-1} (characteristic strong bands).

PMR spectrum (CCl_4): δ 5.5-6.23 (olefinic, 4H, m), 1.5-3 (C-H ring, 6H, en) and 0.93 (CH_3-C-H, 6H, d, J= 7Hz).

Addition of iodine azide to diester (57)

The procedure described by Hassner[70] was followed for the iodine azide addition reactions. To a stirred slurry of sodium azide (0.3 g, 4.8 mmol) in 10 ml of dry acetonitrile in a 50 ml RB flask cooled to -5°, was added freshly prepared iodine monochloride (0.8 g, 6 mmol) over a period of 5 min. The mixture was allowed to stir for a few min. and the diester (57, 1 g, 4 mmol) in acetonitrile (5 ml) was added dropwise. After allowing the reaction mixture to attain room temp., the mixture was stirred for 2 hr. The brownish slurry was poured into water (50 ml) and extracted with ether (25 ml x2). The ethereal extract was washed with 5% sodium thiosulphate followed by brine, dried and stripped of solvent to yield a white solid residue (1.45 g, 90%). Recrystallization from pet ether gave 4-azido-3-iodo-9,10-dicarbomethoxytricyclo[4.2.2.$0^{2,5}$]-dec-7-ene (63) as colourless micro crystals, mp 137°.

IR spectrum (KBr): 2120 (azide), 1740 and 1210 cm^{-1} (ester).

PMR spectrum ($CDCl_3$): δ 6.5 (olefinic, 2H, t), 4.32 (H-C-N_3, 1H, q), 3.61 (CH_3-O-C(=O)-, 6H, s), 3.50 (H-C-I, 1H, q), 2.65-3.55 (C-H ring, 7H, en).

Anal. for $C_{14}H_{16}O_4IN_3$ Calcd: C, 40.28; H,3.83; N,10.07.
Found: C, 40.34; H,3.91; N,10.14.

A mixture of 63 (0.1 g, 0.24 mmol), dimethyl acetylenedicarboxylate (0.5 g, 3.35 mmol) in benzene (15 ml) was refluxed for 4 hr. Removal of solvent and crystallisation from benzene gave the crystalline adduct 64, mp 192-4°.

IR spectrum (KBr): 1740 and 1210 cm^{-1} (ester).

PMR spectrum ($CDCl_3$): δ 6.61 (olefinic, 2H, t), 4.73 (triazolyl methine, and H-C-I, 2H, m), 4.01 (CH_3-O-C(=O)- of triazole, 6H, d), 3.63 (CH_3-O-C(=O)-, 6H, s) and 2.83-3.27 (C-H ring, 6H, en).

Anal. for $C_{20}H_{22}O_8N_3I$ Calcd: C,42.94; H,3.97; N,7.51.
Found: C,43.20; H,4.15; N,7.46.

Addition of iodine azide to 9,10-dimethyltricyclo[4.2.2.$o^{2,5}$]-deca-3,7-diene (59)

(a) In acetonitrile solvent - Iodine azide prepared in situ by the action of iodine monochloride (0.1 g, 0.8 mmol) to sodium azide (50 mg, 0.8 mmol) in acetonitrile (5 ml) was reacted with (0.1 g, 0.6 mmol) of 59 at -5° for 1 hr. Usual work-up gave 0.18 g of a viscous residue. Crystallisation from benzene pet ether (1:4) gave 110 mg (46%) of pale needle

shaped crystals of tetrazole derivative (66), mp 147-8°.

IR spectrum (KBr): 1500, 1450, 1440 cm^{-1} (characteristic -N=N- and -C=N- absorption).

PMR spectrum ($CDCl_3$): δ 4.55 (tetrazolylmethine, 1H, broad s), 3.93 (H-C(I)-I, 1H, s), 2.6 (tetrazolyl methyl, 3H,s), 1.05 (CH_3-C(I)-H, 6H, m).

Anal. for $C_{14}H_{19}N_4I$ Calcd: C,45.41; H,5.18; N,15.13.
Found: C,45.29; H,5.30; N,15.03.

The mother liquor from the crystallisation of tetrazole (66) was concentrated and its ir spectrum and tlc showed the presence of azido iodide (67).

(b) In methylene chloride solvent - Iodine azide prepared in situ by the action of iodine monochloride (0.1 g, 0.8 mmol) on sodium azide (50 mg, 0.8 mmol) in methylene chloride (5 ml) at -5° was reacted with dimethyl compound (59) (0.1 g, 0.6 mmol) for 2 hr. Usual work-up gave 180 mg (88%) of azido iodide 67 as a colourless oil.

IR spectrum (neat): 2110 cm^{-1} (azide).

PMR spectrum (CCl_4): δ 4.16 (H-C(I)-N_3 , 1H, broad s with fine structure), 3.75 (H-C(I)-I, 1H, s), 1.16 (CH_3-C(I)-H, 6H, m), 1.9-3.6 (C-H ring, 8H, en).

Addition of iodine azide to ether (58)

(a) In acetonitrile solvent- Iodine azide prepared in situ by the action of iodine monochloride (0.2 g, 1.6 mmol)

on sodium azide (0.1 g, 1.6 mmol) in acetonitrile (5 ml) was reacted with ether (58', 0.2 g, 1.1 mmol) at -20° for 1 hr. Usual work-up as described earlier furnished 0.35 g of a pale yellow liquid product. This was adsorbed on a silica gel (20 g) column and chromatographed. Elution with benzene gave 70 mg (18%) of azido iodide (69).

IR spectrum (neat): 2120 cm^{-1} (azide).

PMR spectrum (CCl_4): δ4.9 (H-C-N_3, 1H, d, J= 2Hz), 3.4-4.1 (H-C-I & $-CH_2-O-CH_2-$, 5H, m), 1.9-3.5 (CH ring, 8H en).

Further eolution of the column with benzene-ethyl acetate (1:1) furnished 250 mg (56%) of tetrazole (68). Recrystallisation from carbon tetrachloride furnished pale crystalline flakes, mp 152-3°.

IR spectrum (neat): 1515, 1475 and 1400 cm^{-1} (characteristic -N=N- and -C=N- absorption).

PMR spectrum (CCl_4): δ 4.78 (tetrazolyl methine, 1H, broad s), 4.0 (H-C-I, 1H, s), 2.5 (tetrazolylmethyl, 3H, s), 3.4-4.0 ($-CH_2-O-CH_2-$, 4H, m).

Anal. for $C_{14}H_{17}N_4OI$ Calcd: C,43.76; H,4.47; N,14.6.
Found: C,44.09; H,4.39; N,14.38.

(b) In methylene chloride solvent- Iodine azide prepared in situ by the action of iodine monochloride (0.2 g, 1.6 mmol) on sodium azide (0.1 g, 1.6 mmol) in CH_2Cl_2 was

reacted at -5° with 58 (0.2 g, 1.1 mmol). Usual work-up as described earlier gave 69 as a pale oily residue (350 mg, 94%), almost single component by tlc. This was identical in all respects with the minor azido iodide formed in acetonitrile medium.

Methoxymerucuration of diester (57)

To a solution of diester (0.5 g, 2 mmol) in absolute methanol (15 ml), mercuric acetate (0.7 g, 2.2 mmol) was added and the reaction mixture was stirred for 20 hr at room temp. (20°). After the reaction was complete (tlc), methanol was distilled off on a rotary evaporator and the residue was treated with a saturated sodium chloride solution (20 ml). The reaction mixture was further diluted with water (30 ml) and extracted with methylene chloride (25 ml x 2), washed and dried. Removal of solvent gave 1.0 g (96%) of solid methoxymercurial (81). Recrystallisation from benzene-CH_2Cl_2 furnished white crystalline flakes, mp 193-5°.

IR spectrum (KBr): 1740, 1210 cm^{-1} (ester).

PMR spectrum ($CDCl_3$): δ 6.7 (olefinic, 2H, t), 3.6 ($\underline{CH_3}$-O-$\overset{O}{\overset{\|}{C}}$-, 6H, s), 3.23 ($\underline{CH_3}$-O-$\overset{|}{C}$-, 3H, s), 2.6-3.2 (C-$\underline{H}$ ring, 8H, en).

Anal. for $C_{15}H_{19}O_5HgCl$ Calcd: C,34.95; H,3.72.
Found: C,35.03; H,3.86.

Hydroxymercuration of diester (57)

In a small flask, fitted with a magnetic stirrer, was placed 0.7 g (2.2 mmol) of mercuric acetate. A 1:1 mixture of water-THF (15 ml) was added followed by the diester (57, 0.5 g, 2 mmol) in THF (5 ml). The reaction mixture was stirred at room temp. (20°) for 7 hr till the yellow colour was completely discharged. Treatment with saturated brine solution and work-up as described above gave 1.1 g of hydroxymercurial (82) in quantitative yield, mp 164-5°.

IR spectrum (KBr): 3400 (hydroxyl), 1740 and 1210 cm^{-1} (ester).

PMR spectrum ($CDCl_3$): δ 6.71 (olefinic, 2H, t), 4.02 (H-C(-OH)-, 1H, m), 3.61 (CH_3-O-C(=O)-, 6H, s), 2.6-3.45 (C-H ring, 8H, en).

Anal. for $C_{14}H_{17}O_5HgCl$ Calcd: C, 33.55; H, 3.41.
Found: C, 33.52; H, 3.30.

Hydroxymercuration-demercuration[89] of diester (57)

Diester (0.5 g, 2 mmol) in 1:1 water-THF (15 ml) was reacted with mercuric acetate (0.7 g, 2.2 mmol) as described above. After 7 hr at 20°, a solution of 3N sodium hydroxide (5 ml) followed by a mixture of sodium borohydride (50 mg) in 5 ml of 3N NaOH was added. The reduction of the oxymercurial was complete in a few min. and the mercury droplet settled on the base of the reaction flask. Sodium chloride

was added to saturate the aq. layer and extraction was carried out with ether (30 ml x 2). Drying and removal of solvent gave 0.5 g (98%) of 83 as a colourless oil, bp 180-90°(bath, 0.5 mm).

IR spectrum (neat): 3400 (hydroxyl), 1740 and 1200 cm^{-1} (ester).

PMR spectrum (CCl_4): δ 6.3 (olefinic, 2H, t), 3.68 (H-C-OH, 1H, m), 3.51 (CH_3-O-C-, 6H, s), 1.7-3.2 (C-H ring, 9H, en)

Anal. for $C_{14}H_{18}O_5$ Calcd: C, 63.14; H, 6.81.
Found: C, 62.99; H, 6.89.

Chromium trioxide-pyridine oxidation[90] of 9,10-dicarbomethoxy-tricyclo[4.2.2.$o^{2,5}$]dec-7-en-3-ol (83)

A solution of alcohol (83, 0.5 g, 1.9 mmol) in pyridine (5 ml) was added dropwise to an efficiently stirred slurry of CrO_3-pyridine complex (prepared from CrO_3 1 g in pyridine 5 ml) cooled in an ice bath. After stirring for 3 hr the reaction mixture was poured into water and extracted with ether (20 ml x 2). Washing, drying and removal of solvent gave 0.4 g (80%) of dicarbomethoxytricyclo[4.2.2.$o^{2,5}$]-dec-7-en-3-one (84). Recrystallisation from pet ether-benzene (4:1) gave white micro needles, mp 94° (lit.[89] 93-5°).

IR spectrum (KBr): 1775 (cyclobutanone), 1745 and 1200 cm^{-1} (ester).

PMR spectrum ($CDCl_3$): δ 6.63 (olefinic, 2H, t), 3.63 ($\underline{CH_3}$-O-$\overset{O}{\overset{\|}{C}}$-, 6H, s), 2.6-3.43 (C-$\underline{H}$ ring, 7H, en).

Mercuration of diester (57) in presence of azide ion

A mixture of diester (57, 0.5 g, 2 mmol), mercuric acetate (0.7 g, 2.2 mmol) and sodium azide (0.15 g, 2.4 mmol) in methanol (15 ml) was stirred at room temp. (20°) for 15 hr. The solvent was removed under reduced pressure and the residue was treated with saturated brine solution. Extraction with CH_2Cl_2 (25 ml x 2), removal of solvent and crystallisation from benzene-pet ether (4:1) gave 1 g (95%) of azido mercurial (85), mp 155-7°.

IR spectrum (KBr): 2120 (azide), 1740, 1210 cm^{-1} (ester).

PMR spectrum ($CDCl_3$): δ 6.48 (olefinic, 2H, t), 3.82 ($\underline{H}$-$\overset{|}{\underset{|}{C}}$-$N_3$, 1H, m), 3.58 ($\underline{CH_3}$-O-$\overset{O}{\overset{\|}{C}}$-, 6H, s), 2.7-3.2 (C$\underline{H}$ ring, 7H, en).

Anal. for $C_{14}H_{16}O_4N_3HgCl$: Calcd: C,31.94; H,3.07; N,7.99.
Found: C,32.08; H,3.23; N,8.01.

A mixture of azido mercurial (85) (0.1 g, 0.2 mmol) and dimethyl acetylenedicarboxylate (0.5 g, 3.5 mmol) in dry benzene (10 ml) was refluxed for 6 hr. Removal of solvent and crystallisation from benzene gave 0.11 g of the crystalline adduct 86, mp 210-12°.

IR spectrum (KBr): 1740 and 1200 cm^{-1} (ester).

Anal. for $C_{20}H_{22}O_8N_3HgCl$ Calcd:C,35.93;H,3.32;N,6.29.
Found:C,36.18;H,3.04;N,6.50.

Iodination of azido mercurial (86) with I_2 and triiodide ion

To a solution of azido mercurial (86 , 0.45 g, 0.9 mmol) in dioxane (10 ml) was added 300 mg of iodine crystals and the mixture was left aside at room temp. (20°) for 4 hr. The reaction mixture was poured into water, extracted with CH_2Cl_2 (25 ml x 2) and washed successively with 10% sodium thiosulphate and brine. Removal of solvent and crystallisation from pet ether gave 0.35 g (98%) azido iodide (63), mp 137°. This compound was identical (mixed mp, ir) with the azido iodide obtained from IN_3 addition to 57. Repetition of the above experiment in aq. dioxane and in presence of potassium iodide lead to exactly identical results.

Methoxymercuration of ether (58)

A mixture of ether (58 , 0.1 g, 0.6 mmol) and mercuric acetate (225 mg, 0.7 mmol) in absolute methanol (5 ml) was stirred at room temp. for 1 hr. Usual work-up as described for 57 and crystallisation from benzene gave 0.21 g (82%) of methoxymercurial (87), mp 179-80°.

IR spectrum (KBr): 1100, 920 cm^{-1} (ether).

PMR spectrum ($CDCl_3$): δ 6.56 (olefinic, 2H, broad t), 3.53 (H-C-OMe, 1H, m), 3.23 (CH_3-O-C-, 3H, s), 3.47 & 3.86 ($-CH_2-O-CH_2$, 4H, a pair of t, J=8Hz), 2.1-3.0 (C-H ring,8H,2n).

Anal. for $C_{13}H_{17}O_2HgCl$ Calcd: C, 35.38; H, 3.89.
Found: C, 35.81; H, 3.56.

Hydroxymercuration of ether (58)

A mixture of ether (58 , 0.45 g, 1.5 mmol),mercuric acetate (0.2 g, 1.1 mmol) in 1:1 water-THF (10 ml) was stirred at room temp. for 3 hr. Work-up as described earlier gave 0.4 g (81%) of hydroxymercurial(89), mp 182-3°.

IR spectrum (KBr): 3650 (hydroxyl), 1050 & 915 cm^{-1} (ether).

PMR spectrum ($CDCl_3$): δ 6.58 (olefinic, 2H, diffused t), 4.52 (H-C-OH, 1H, q), 2.1 (-OH, 1H, s), 3.2-4 ($-CH_2-O-CH_2-$ & H-C-HgCl, 5H, m), 2-3.1 (C-H ring, 6H, en).

Anal. for $C_{12}H_{15}O_2HgCl$ Calcd: C, 33.73; H, 3.55.
Found: C, 34.06; H, 3.73.

Hydroxymercuration-demercuration[89] of ether (58)

A mixture of ether (58 , 0.4 g, 2.2 mmol) and mercuric acetate (0.9 g, 2.8 mmol) in 1:1 water-THF (15 ml) was stirred at room temp. for 3 hr. Sodium hydroxide (5 ml, 3N) and sodium borohydride (125 mg) in aq. NaOH (5 ml, 3N) were added to the reaction mixture and stirring continued for 1 hr.Usual work-up as described above gave 0.37 g (84%) of the alcohol (91), bp 150-60° (bath, 2 mm); mp 89-90°.

IR spectrum (KBr): 3550 (hydroxyl), 910 cm^{-1} (ether).

PMR spectrum ($CDCl_3$): δ 6.30 (olefinic, 2H, t), 4.05-3.2 (-$\underline{CH_2}$-O-$\underline{CH_2}$- & $\underline{H}$-C-OH, 5H, m), 2.85-1.80 (C-$\underline{H}$ ring, & -O-$\underline{H}$, 8H, en).

Anal. for $C_{12}H_{16}O_2$ Calcd: C, 74.95; H, 8.40.
Found: C, 74.69; H, 8.77.

Chromium trioxide-pyridine oxidation[90] of 91

The alcohol (91 , 0.25 g, 1.3 mmol) in pyridine (5 ml) was added to a stirred slurry of CrO_3-pyridine complex (prepared from 0.5 g CrO_3 in 5 ml of pyridine) in an ice bath. The reaction was terminated after 1 hr by pouring into water and organic material was extracted with CH_2Cl_2 (25 ml x 2) washing, drying and removal of solvent gave 0.2 g (80%) of ketone (93), bp 130-35° (bath, 2 mm); mp 62°.

IR spectrum (KBr): 1780 (cyclobutanone), 1020 cm^{-1} (ether).

PMR spectrum ($CDCl_3$): δ 6.21 (olefinic, 2H, t), 4.1-3.2 (-$\underline{CH_2}$-O-$\underline{CH_2}$-, 4H, m), 3.1-2.0 (C-$\underline{H}$ ring, 7H, en).

Anal. for $C_{12}H_{14}O_2$ Calcd: C, 75.75; H, 7.43.
Found: C, 75.90; H, 7.61.

Methoxymercuration of 9,10-dimethyltricyclo [4.2.2.$0^{2,5}$]-deca-3,7-diene (59)

A mixture of dimethyl compound (59) (0.1 g, 0.6 mmol) and mercuric acetate (225 mg, 0.7 mmol) in absolute methanol (5 ml) was stirred at room temp. for 1 hr. Usual work-up as

already described and crystallisation from benzene gave 0.22g (62%) of the methoxymercurial (88), mp 126-7°.

IR spectrum (KBr): 1060, 1100 cm^{-1} (ether).

PMR spectrum ($CDCl_3$): δ 6.53 (olefinic, 2H, t), 3.5 (H-C-OMe, 1H, m), 3.2 (CH_3-O-C-, 3H, s), 0.83 (CH_3-C-H, 6H, m), 1.7-2.9 (C-H ring, 7H, en).

Anal. for $C_{13}H_{19}OHgCl$ Calcd: C, 36.52; H, 4.49.
Found: C, 36.77; H, 4.38.

Hydroxymercuration of 59

A mixture of 59 (0.16 g, 1 mol) and mercuric acetate (0.35 g, 1.1 mmol) in 1:1 water-THF (10 ml) was stirred at room temp. for 3 hr. Usual work-up furnished 0.35 g (85%) of hydroxymercurial (90), mp 137-38°.

IR spectrum (KBr): 3450 and 1020 cm^{-1} (hydroxyl).

PMR spectrum ($CDCl_3$): δ 6.55 (olefinic, 2H, m), 4.5 (H-C-OH, 1H, m), 3.9 (H-C-HgCl, 1H, m), 2.03 (-OH, 1H, s), 0.78 (CH_3-C-H, 6H, d, 6.5 Hz), 1.6-3.0 (C-H ring, 6H, en).

Anal. for $C_{12}H_{17}OHgCl$ Calcd: 34.87; H, 4.15.
Found: 35.12; H, 4.23.

Hydroxymercuration-demercuration[89] of 59

The hydrocarbon (59 , 0.35 g, 2.2 mmol) and mercuric acetate (0.8 g, 2.5 mmol) in 1:1 water-THF was stirred for 3 hr at room temp. A 3N solution of sodium hydroxide (5 ml)

followed by sodium borohydride (75 mg) in 3N aq. NaOH (5 ml) was added and stirring continued for a further period of 1 hr. Usual work-up gave 0.32 g (82%) yield of 9,10-dimethyltricyclo[4.2.2.$0^{2,5}$]dec-7-en-3-ol (92), bp 120-25° (bath, 2 mm).

IR spectrum (neat): 3540 cm^{-1} (hydroxyl).

PMR spectrum ($CDCl_3$): δ 6.30 (olefinic, 2H, t), 3.80 (H-C-OH, 1H, t), 0.77 ($-CH_3$, 6H, d, J=6 Hz).

Anal. for $C_{12}H_{18}O$ Calcd: C, 80.83; H, 10.19.
Found: C, 80.51; H, 9.96.

Chromium trioxide-pyridine oxidation[90] of 9,10-dimethyltricyclo[4.2.2.$0^{2,5}$]dec-7-en-3-ol (92)

The alcohol (92, 0.2 g) in pyridine (5 ml) was oxidised with CrO_3-pyridine reagent as described earlier. Usual work-up gave 0.16 g (80%) of 9,10-dimethyltricyclo[4.2.2.$0^{2,5}$]-dec-7-en-2-one (94), bp 100-110° (bath, 2 mm).

IR spectrum (neat): 1780 cm^{-1} (cyclobutanone).

PMR spectrum ($CDCl_3$): δ 6.20 (olefinic, 2H, t), 0.77 ($-CH_3$, 6H, d, J=6Hz), 2.8-1.8 (C-H ring, 7H, en).

Addition of benzenesulphenyl chloride to diester (57)

To a stirred solution of diester (57, 0.25 g, 1 mmol) in methylene chloride (10 ml), containing suspended calcium carbonate (50 mg) was added benzenesulphenyl chloride (0.2 g, 1.4 mmol) in benzene (2 ml) at -20°. The reaction mixture

was first stirred at -20° for 30 min and then at room temp. for 1 hr. The reaction mixture was poured into water (10 ml), extracted with methylene chloride (20 ml x 2) and washed with 10% sodium hydroxide solution (10 ml x 2). The solvent was removed to yield 0.4 g of crude mixture of adducts (100) and (101). This material was absorbed on a silica gel column (25 g) and chromatographed. Elution with benzene gave 0.22 g (62%) of trans adduct (100), which was recrystallised from carbon tetrachloride to furnish white silky crystals, mp 119-20°.

IR spectrum (KBr): 1740, 1210 (ester), 740 cm^{-1}.

PMR spectrum ($CDCl_3$): δ 7.25 (phenyl, 5H, br s), 6.46 (olefinic, 2H, m), 4.42 (H-C-Cl, 1H, t), 3.7 (H-C-S-Ph, 1H, t), 3.56 (H_3C-O-C(=O)-, 6H, s).

Anal. for $C_{20}H_{21}O_4SCl$: Calcd: C, 61.14; H, 5.38.
Found: C, 61.25; H, 5.37.

Further elution of the column with benzene--ethylacetate (1:1) gave 70 mg (20%) of cis adduct (101) crystallisation from carbon tetrachloride furnished colourless crystals, mp 201-3°.

IR spectrum (KBr): 1740, 1215 (ester) and 755 cm^{-1}.

PMR spectrum ($CDCl_3$): δ 7.5 (phenyl, 5H, br s), 6.55 (olefinic, 2H, t), 4.9 (H-C-Cl, 1H, t), 3.6 (CH_3-O-C(=O)-, 6H, s).

Anal. for $C_{20}H_{21}O_4SCl$ Calcd: C, 61.14; H, 5.38.
Found: C, 60.79; H, 5.26.

Benzenesulphenyl chloride addition to ether (58)

To a stirred solution of ether (58, 0.2 g, 1.1 mmol) in methylene chloride (10 ml, containing suspended calcium carbonate (50 mg), was added benzenesulphenyl chloride (0.2 g, 1.4 mmol) in benzene (2 ml) at -20°. The reaction mixture was first stirred at -20° for 1 hr and then at room temperature for 1 hr. The reaction mixture was poured into water (10 ml), extracted with methylene chloride (20 ml x 2) and washed with 10% sodium hydroxide solution (10 ml x 2). The solvent was removed to yield 0.35 g of crude mixture of adducts (102) and (103). This material was adsorbed on a silica gel column (25 g) and chromatographed. Elution with benzene gave 0.23 g (63%) of trans adduct (102) which was recrystallised from carbon tetrachloride to furnish white crystals, mp 143-44°.

IR spectrum (KBr): 3050, 1575, 1015 (ether), and 740 cm^{-1}.

PMR spectrum ($CDCl_3$): δ7.28 (phenyl, 5H, m), 6.39 (olefinic, 2H, m), 4.5 (H-C(-Cl)-, 1H, t), 3.2-4.1 ($-CH_2-O-CH_2-$ & H-C(-)-S-, 5H, en).

Anal. for $C_{18}H_{19}OSCl$ Calcd: C, 67.81; H, 6.00.
Found: C, 67.95; H, 5.81.

Further elution of the column with benzene-ethyl acetate (1:1) gave 65 mg (18%) cis adduct (103), which was crystallised from carbon tetrachloride to furnish white flakes, mp 152-53°.

IR spectrum (KBr): 3060, 1520, 1050 (ether) and 745 cm^{-1}.

PMR spectrum ($CDCl_3$): δ 7.5 (phenyl, 5H, br s), 6.35 (olefinic, 2H, t), 4.88 (H-C(Cl)-, 1H, t), 3.1-4.0 ($-CH_2-O-CH_2-$ & H-C(S)-, 5H, en).

Anal. for $C_{18}H_{19}OSCl$ Calcd: C, 67.81; H, 6.00.
Found: C, 67.57; H, 6.21.

Benzenesulphenyl chloride addition to dimethyl compound (59)

To a stirred solution of dimethyl compound (59, 0.25 g, 1.56 mmol) in methylene chloride (10 ml), containing calcium carbonate (50 mg) was added benzenesulphenyl chloride (0.3 g, 2.1 mmol), in benzene (2 ml) at -20°. The reaction mixture was stirred for 2 hr at -20° and then warmed up to the room temp. It was poured into water (10 ml), extracted with methylene chloride (20 ml x 2) and washed with 10% sodium hydroxide solution (10 ml x 2). The solvent was removed to yield 0.4 g of crude mixture of adducts (104) & (105). This material was adsorbed on a silica gel column (25 g) and eluted with pet ether to get 0.285 g (60%) of trans adduct (104). It was crystallised from pet ether, which gave white crystals, mp 86°.

IR spectrum (KBr): 3040, 1580, 1475, 735, 710 and 685 cm^{-1}.

PMR spectrum (CCl_4): δ 7.2 (phenyl, 5H, m), 6.33 (olefinic, 2H, m), 4.37 (H-C-Cl, 1H, q), 3.65 (H-C-S-, 1H, t), 0.77 ($-CH_3$, 6H, d).

Anal. for $C_{18}H_{21}SCl$ Calcd: C, 70.92; H, 6.96.
Found: C, 70.59; H, 6.91.

Further elution of the column with benzene and ethyl acetate (1:1) only gave mixtures and corresponding cis-adduct (105) could not be obtained from the column.

Nitrosyl chloride addition to diester (57)

The diester (57 , 1 g, 4 mmol) was dissolved in methanol (15 ml) and cooled to -5°. Isoamylnitrite (7 ml, 16.5 mmol) was added followed by careful addition of conc. HCl (4 ml) with vigorous sttrring. The stirring was continued for 4 hr and the reaction mixture poured into ice water. Extraction with ether (25 ml x 2), washing and drying furnished 1.2 g (90%) of chlorocyclobutanone(117), mp 164-65°.

IR spectrum (KBr): 1780 (cyclobutanone), 1745, 1210 cm^{-1} (ester).

PMR spectrum ($CDCl_3$): δ 6.44 (olefinic, 2H, t), 4.26 (H-C-Cl, 1H, t, J= 4Hz), 3.7 (CH_3-O-C(=O)-, 6H, s), 2.64-3.6 (C-H ring, 6H, en).

Anal. for $C_{14}H_{15}O_5Cl$ Calcd: C, 56.28; H, 5.07.
Found: C, 56.56; H, 5.40.

Hydroboration[88] of diester (57)

The diester (57 , 0.5 g, 2 mmol) in dry THF (25 ml) was cooled in an ice bath and sodium borohydride (0.2 g, 5 mmol) and acetic acid (300 mg) were added with rapid stirring.After 4 hr 20% NaOH (5 ml) and 4 ml of 30% H_2O_2 were carefully added and stirring continued for another 1 hr. Extraction with CH_2Cl_2 (25 ml x 2), washing and drying gave 0.51 g (96%) of alcohol (83) identical with the oxymercuration-demercuration product of diester (57)

Addition of chlorosulphonyl isocyanate to diester (57)

To a CH_2Cl_2 (5 ml) solution of diester (57) (0.3 g, 1.2 mmol) cooled in an ice bath, chlorosulphonyl isocyanate (0.3 g) in 2 ml of CH_2Cl_2 was added. The reaction mixture was stirred over night at room temperature and CH_2Cl_2 evaporated under reduced pressure. Crystallisation from acetone-benzene mixture gave 0.22 g (82%) of an anhydride, which is identical with COT-maleic anhydride adduct (60), mp & mmp 168^{o}.[65]

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CHAPTER II

NOVEL TRANSANNULAR CYCLISATIONS OF TRICYCLO $[4.2.2.0^{2,5}]$ DECA-3,7-DIENE RING SYSTEM

II.1 ABSTRACT

The addition of bromine, pyridinium hydrobromide perbromide, iodobenzene dichloride, iodine monochloride and iodine nitrate to 9,10-dicarbomethoxytricyclo $[4.2.2.0^{2,5}]$ deca-3,7-diene (27) has been investigated. The results of addition of bromine to 27 are at variance with those reported in literature. These electrophilic additions proceed via a novel transannular cross bonding of the proximal double bonds. Structures of the resulting cage-like compounds 38, 43 & 44 have been deduced through incisive spectral analysis. Reaction of 27 with m-chloroperbenzoic acid furnished the epoxide (45) in good yield. Acid catalysed rearrangement of 45 proceeded with transannular π participation to yield

the tetracyclic alcohol 46. Structures of several compounds, previously reported in literature, have been revised.

II.2 INTRODUCTION

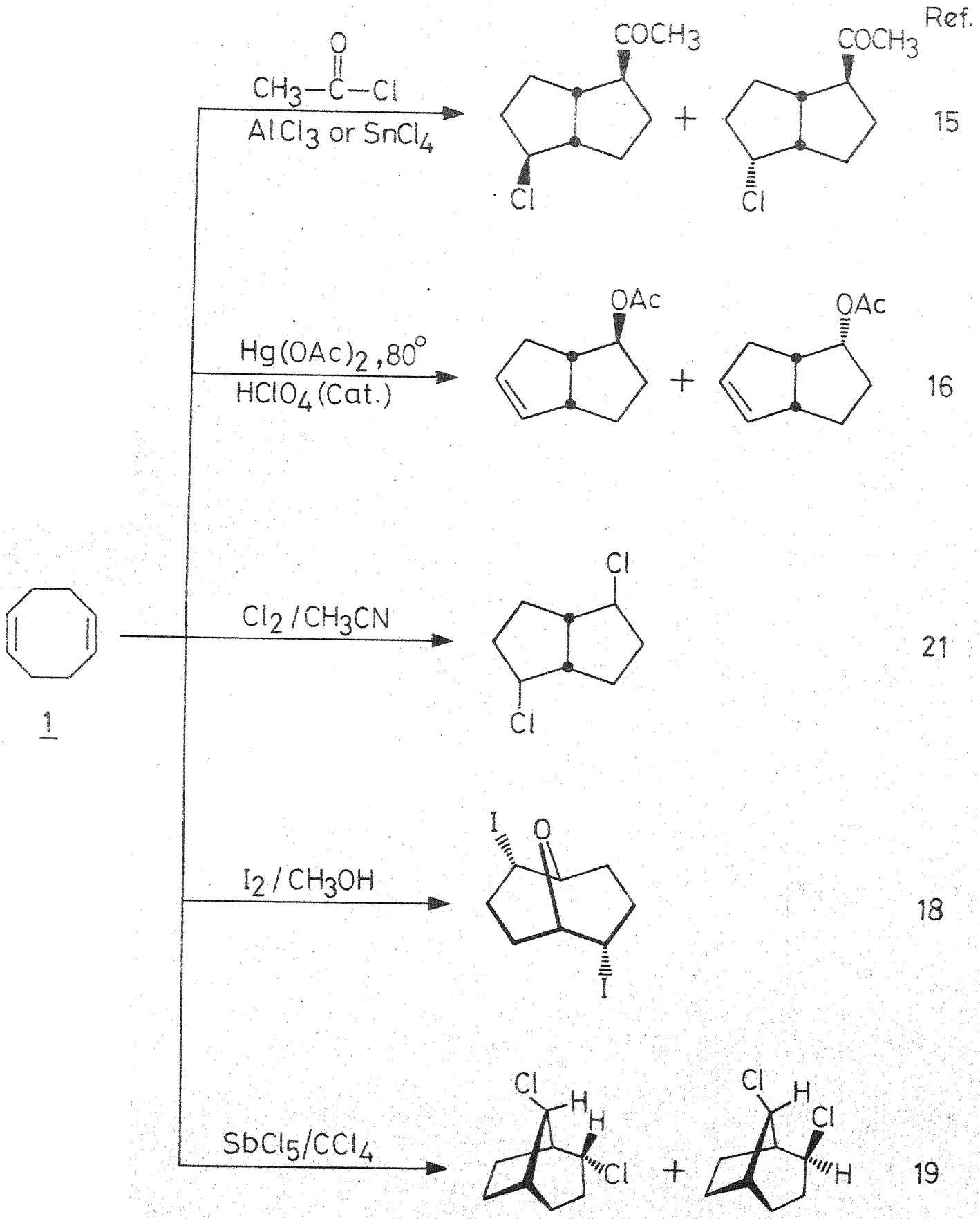
Over the years, it has been amply demonstrated that certain molecules possessing isolated π bonds in close proximity can provide convenient route to a variety of polycyclic molecules of current interest.[1-3] The most commonly encountered reactions of such proximal π systems are the photochemical ring closure and electrophile induced cationic cyclisation. The photochemical reactions are usually intramolecular $\pi_s^2 + \pi_s^2$ cycloadditions leading to cage-type, space-enclosing molecules.[4-6] In fact, much of the success achieved in the synthesis[7-9] of strained polycyclic compounds can be attributed to these transannular photo-cycloadditions and their importance needs little testimony. The electrophile induced cyclisation, on the other hand, leads to the formation of either functionalised half-cage systems or cyclic products of much synthetic value.[10-12] As the subject matter of this chapter is concerned with the electrophile induced transannular cyclisations of a polycyclic diene, a few relevent examples from literature are cited here.

Among the various types of organic molecules, the medium ring dienes and bridged polyclic dienes possessing isolated π bonds in favourable geometrical disposition, are

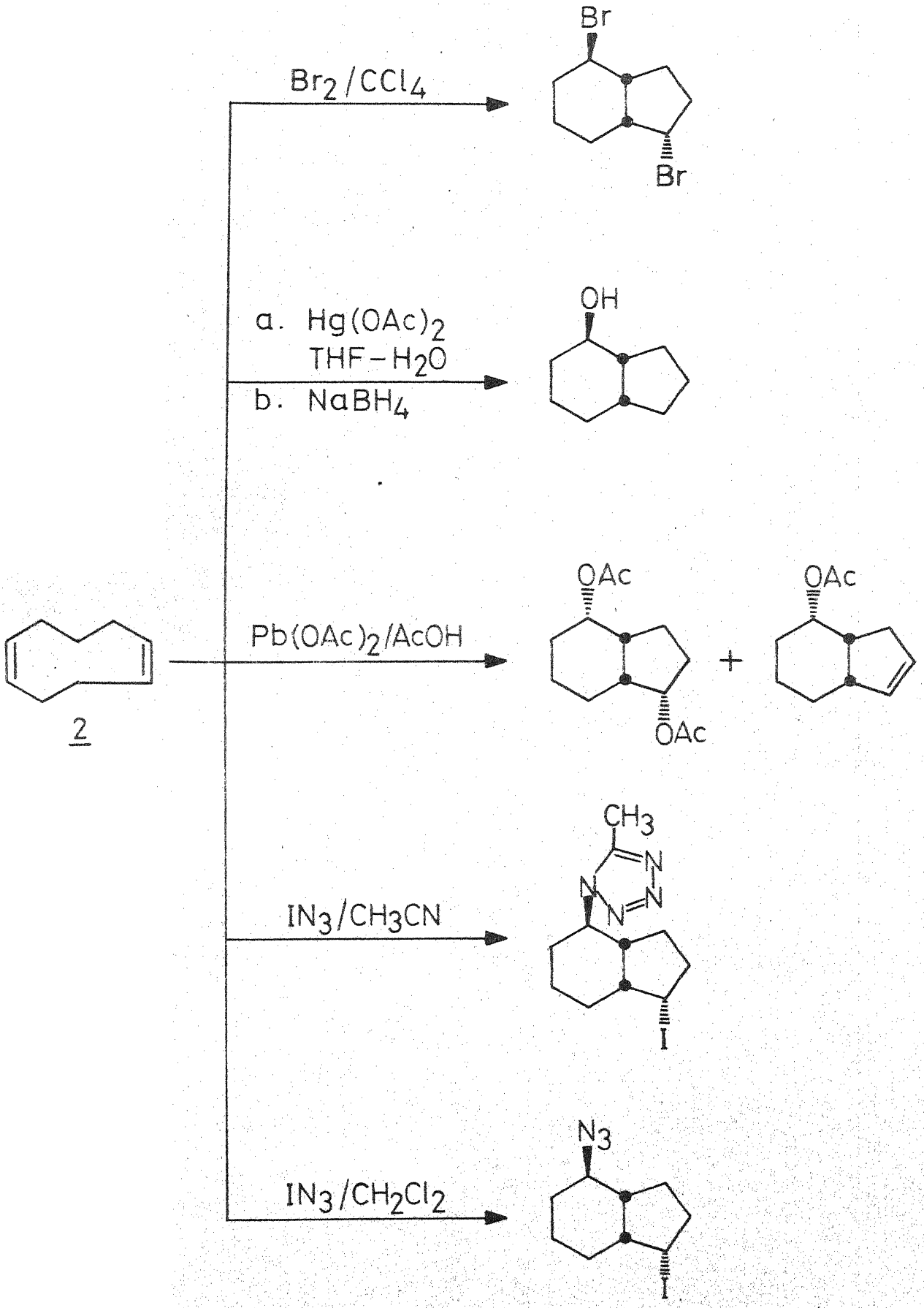
most amenable to transannular reactions.[1,2] A unique feature of medium rings (C_8-C_{11}) is the existence of certain conformations in which the opposite sides of the ring come in close proximity to each other. The existence of such conformations was brilliantly demonstrated, in early fifties, by Professors Cope[2,13] and Prelog[14] through the discovery of facile transannular hydride shifts during the carbonium ion reactions of cyclooctane and cyclodecane derivatives. Later studies[1,2] revealed that transannular participation by a double bond can also occur with great ease to furnish bicyclic compounds. This led to extensive investigation of reactions of medium ring dienes among which cis,cis-1,5-cyclooctadiene[15-21] (1), cis,cis-1,5-cyclononadiene[22,23] (2) and cis,trans-1,5-cyclodecadiene[23-26] (3) were the main focus of attention. Some selected examples of cyclisation reactions of dienes 1, 2 & 3 with various electrophiles are provided in Schemes II.1, II.2 and II.3 respectively.

Many bridged polycyclic molecules are also endowed with favourable spatial orientation of isolated olefinic bonds, suitable for transannular interactions. This was first demonstrated by Cristol and Snell[27,28] in bicyclo[2.2.1]hepta-2,5-diene chemistry through photoisomerisation of norbornadiene derivative 4 to quadricyclane ring system 5 (Scheme II.4). Other early examples of transannular participation in bridged systems emanated from the carbonium ion reactions of norbornadiene[29-31] (6), norbornadiene-cyclopentadiene adduct[31-34] (7)

Scheme II.1

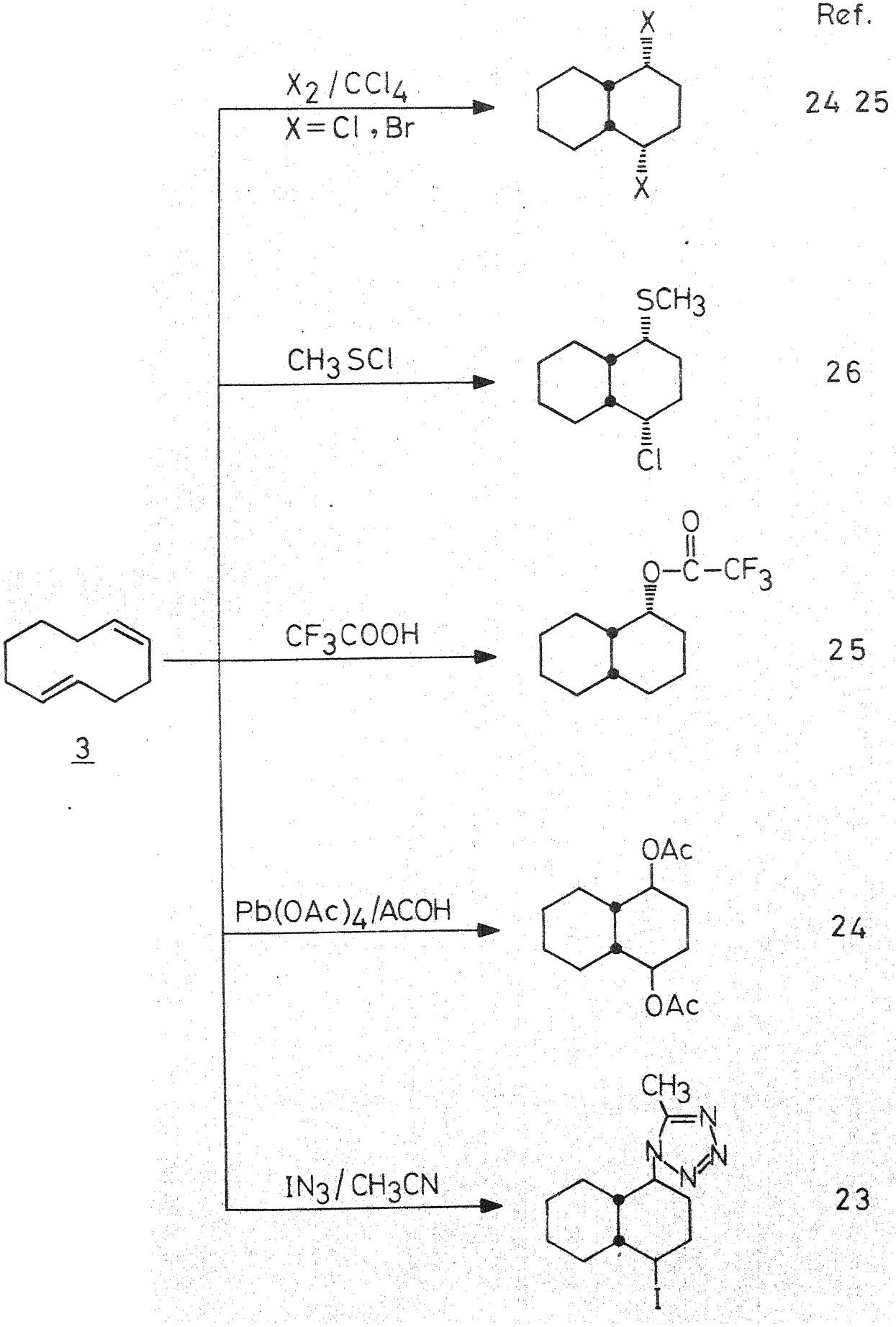

Ref.
CH3–C(=O)–Cl
AlCl3 or SnCl4
COCH3
COCH3
Cl
Cl
15
Hg(OAc)2, 80°
HClO4 (Cat.)
OAc
OAc
16
1
Cl2 / CH3CN
Cl
Cl
21
I2 / CH3OH
I
O
I
18
SbCl5/CCl4
Cl
H
H
Cl
Cl
H
Cl
H
19

Scheme II.2

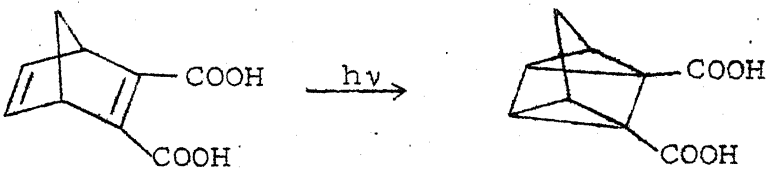


	Ref.
	22
	22
	22
	23
	23

Scheme II.3


Ref.
X2 / CCl4
X = Cl , Br
24 25
CH3 SCl
26
CF3COOH
25
3
Pb(OAc)4/ACOH
24
IN3 / CH3CN
23

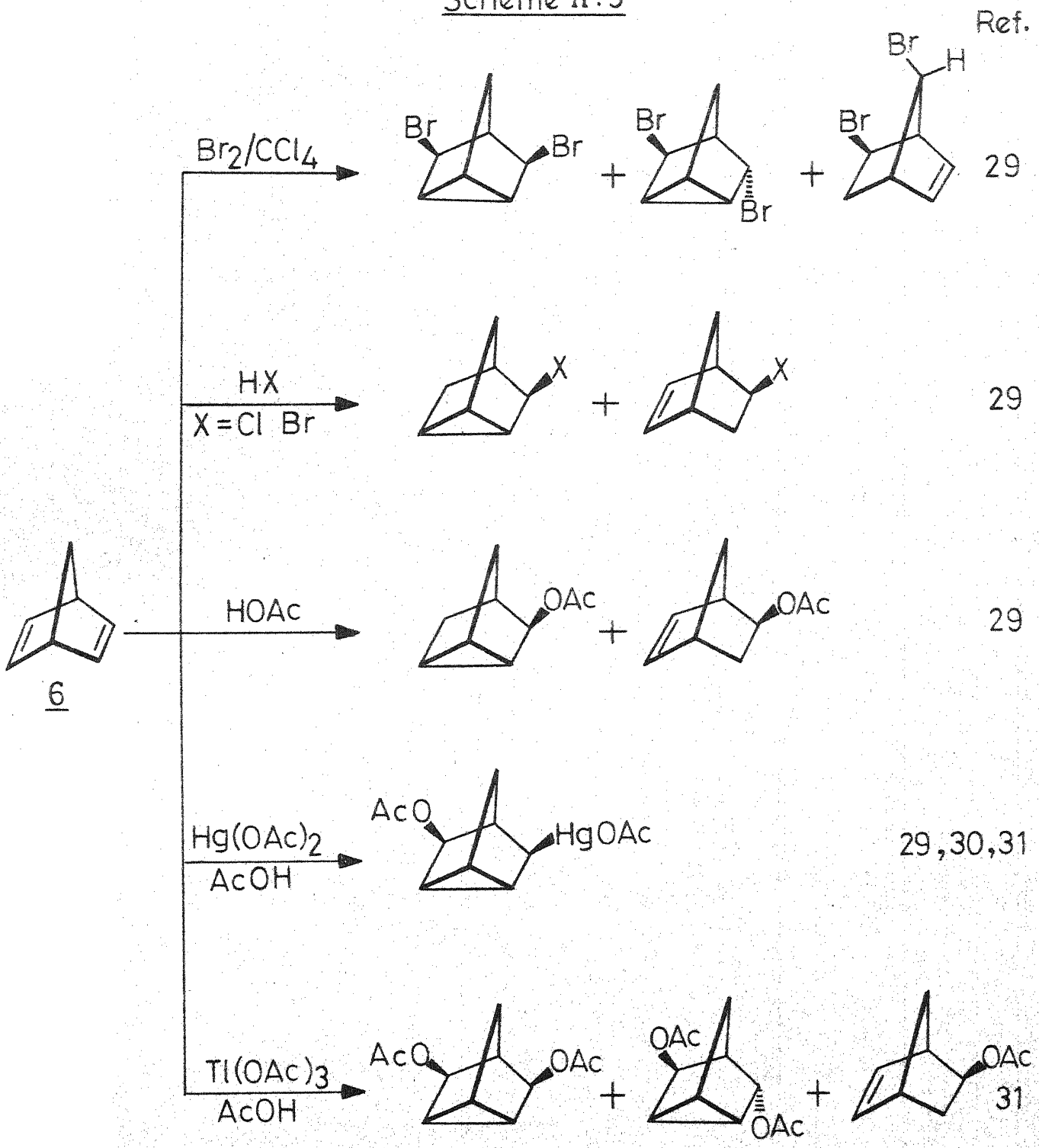
Scheme II.4



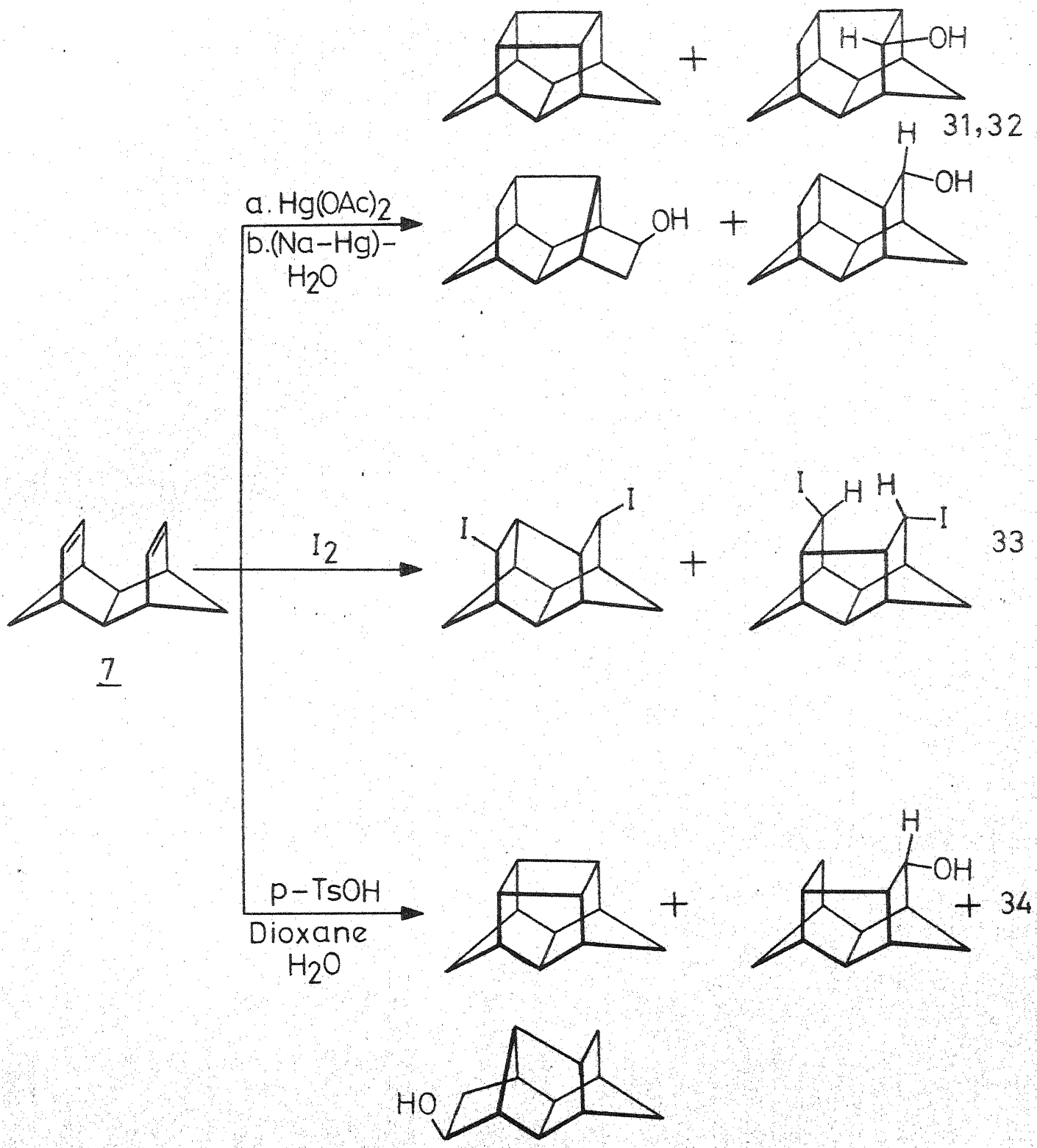
4 5

and its chlorinated analogue[33,35] (8, isodrin). The results of addition of various electrophiles to 6, 7 & 8 are summarised in Schemes II.5, II.6 and II.7 respectively. Some of these reactions have found interesting applications in complex organic synthesis and in the study of neighbouring group participation. Recent examples of transannular π participation (Scheme II.8) include an elegant preparation[10] of trishomocubane derivative 10 via bromination of tetracyclic diene (9) and cyclisation[11] of barbaralone (11) to a mixture of bromides 12 & 13. An unusual example[36] of facile cyclisation is the formation of alcohols 15, 16 & 17 during oxymercuration of novel hydrocarbon, 9,10-benzotricyclo$\left[4.2.2.2^{2,5}\right]$-dodeca-3,7,9-triene (14). In another context, the exo,exo, configuration of basketene-maleic anhydride adduct (18) was elucidated[37] via bromination-lactonisation to 19 (Scheme II.9). Finally, many of the electrophilic additions[38-41] to hexamethyl Dewar benzene (20), in a formal sense, belong to this category as exemplified by the formation of seco-prismane derivative 21 as shown in Scheme II.10.

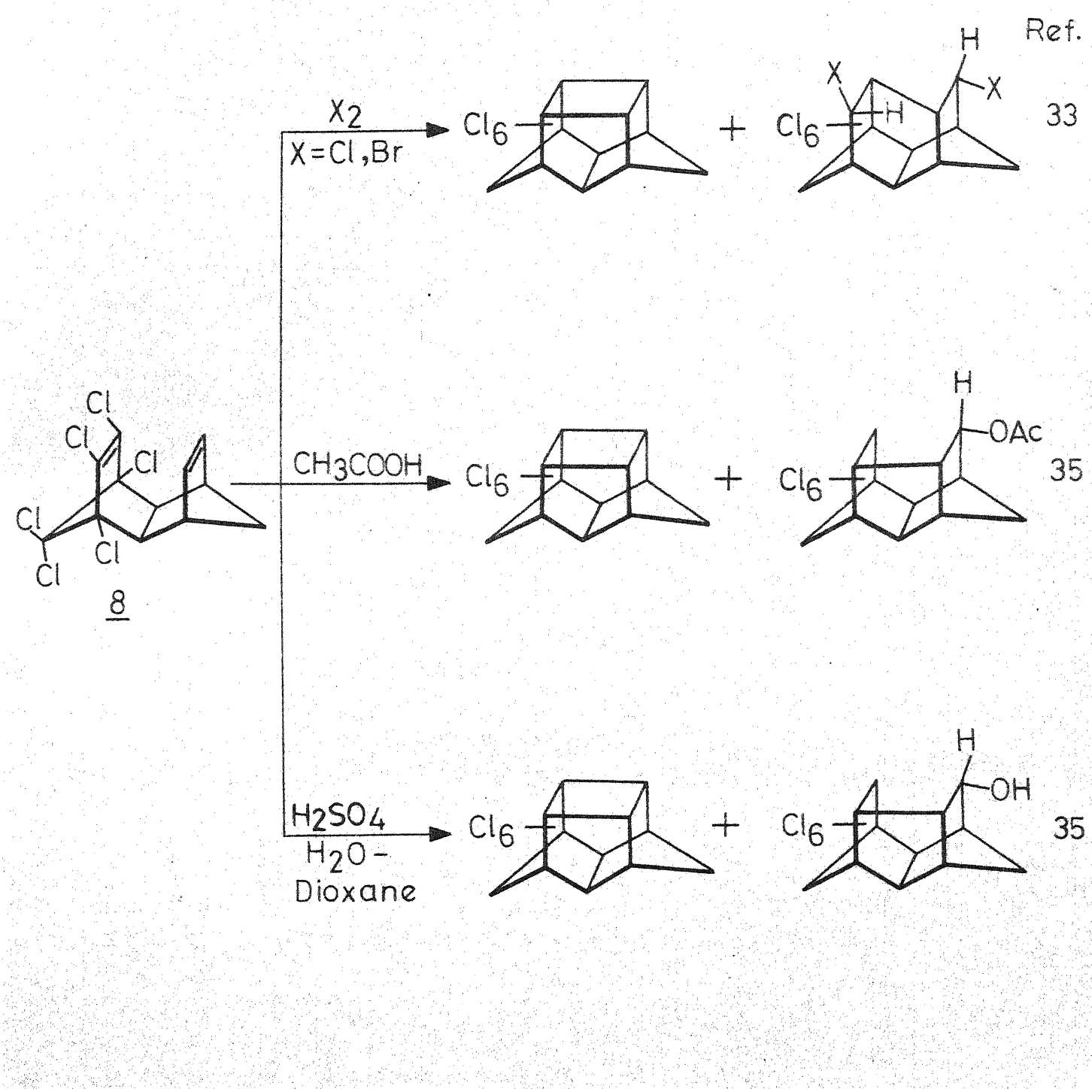
Scheme II.5


Ref.
Br2/CCl4
Br
Br
Br
Br
Br
H
29
HX
X=Cl Br
X
X
29
HOAc
OAc
OAc
29
6
Hg(OAc)2
AcOH
AcO
HgOAc
29,30,31
Tl(OAc)3
AcOH
AcO
OAc
OAc
OAc
OAc
31

Scheme II.6

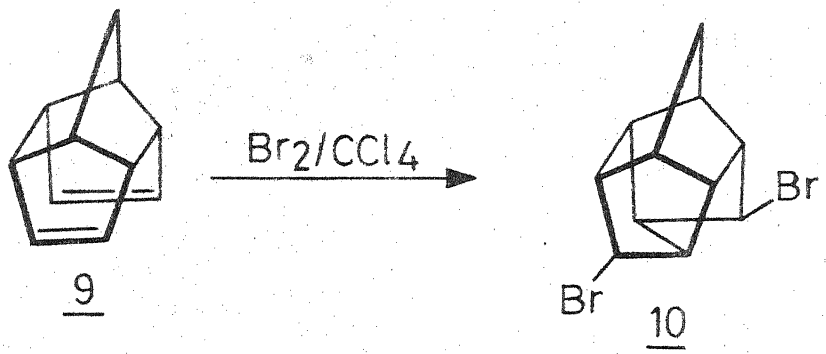

Ref.
H
OH
31,32
a. Hg(OAc)2
b.(Na-Hg)-
H2O
OH
H
OH
I2
I
I
I H H
I
33
7
p-TsOH
Dioxane
H2O
H
OH
34
HO

Scheme II.7

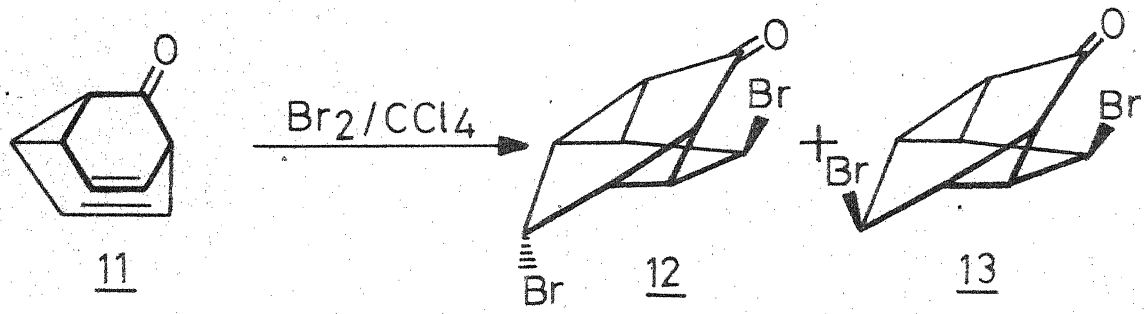

Ref.
X2
X=Cl,Br
Cl6
H
X
X
H
33
Cl
Cl
Cl
Cl
Cl
Cl
8
CH3COOH
Cl6
H
OAc
35
H2SO4
H2O-
Dioxane
Cl6
H
OH
35

Scheme II. 8

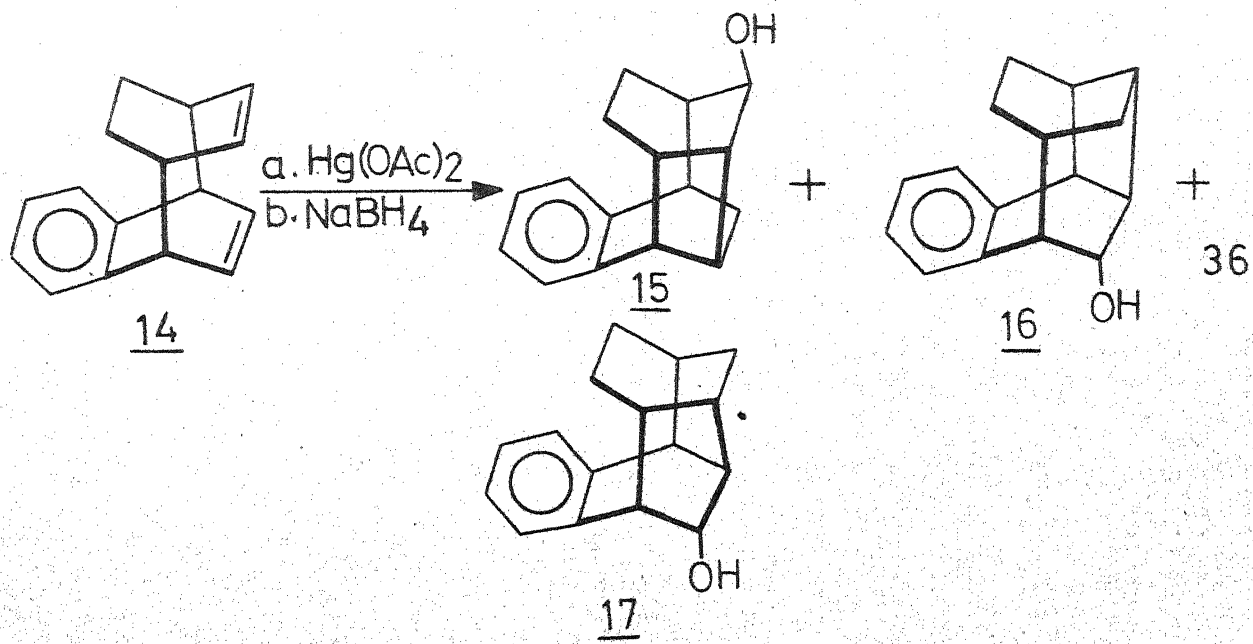
Ref



9 10 10

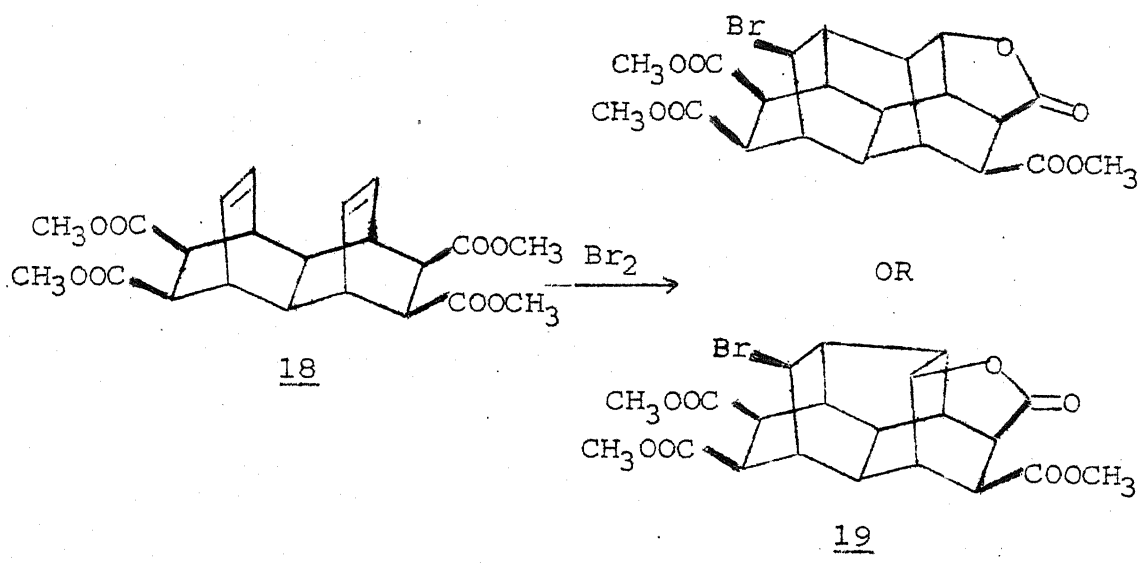


11 11 12 13



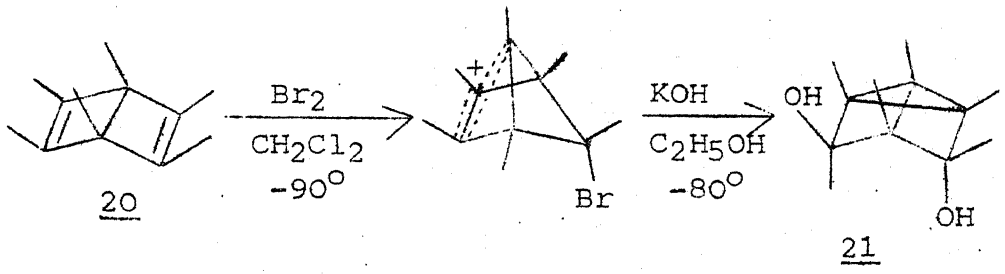
14 15 16 17 36

Scheme II.9



18 19

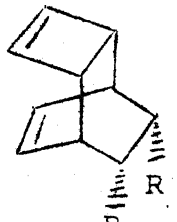
Scheme II.10



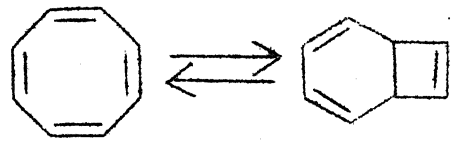
20 21

The tricyclo [4.2.2.$o^{2,5}$] deca-3,7-diene ring system 22, readily available[42,43] from cyclooctatetraene (COT, 23) via the diene synthesis, is endowed with a unique disposition of π bonds ideally suited for the study of proximity effects and transannular reactions. The addition of bifunctional electrophiles, such as halogens and pseudo halogens, to 22 is expected to proceed with transannular π participation and

eventuate in tetracyclic cage compounds of the type 24, 25, 26, etc. However, addition of electrophiles to system 22 has

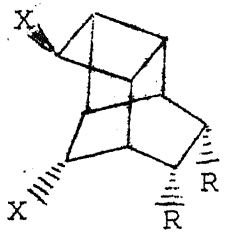


22, R=H

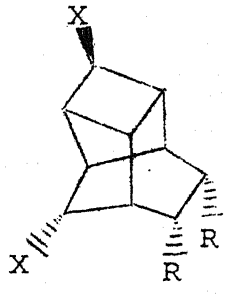


23

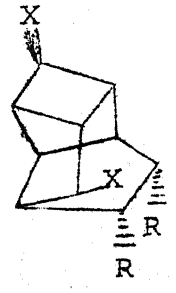
only received isolated attention. During his classical researches on COT, Reppe[42] studied the UV catalysed addition of bromine to diester (27) and reported the isolation of a bromolactone, mp 179° and a dibromide, mp 227°. No structure was assigned to the dibromide and the bromolactone was erroneously recognised as 28. In a subsequent reinvestigation,



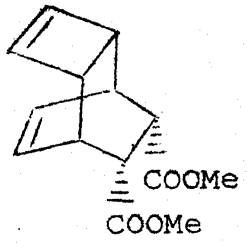
24, R=H. X=halogen



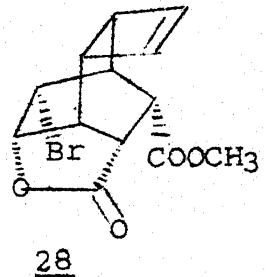
25, R=H, X=halogen



26, R=H, X=halogen

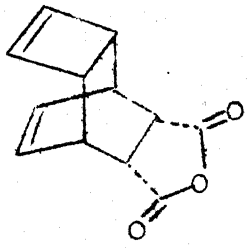


27

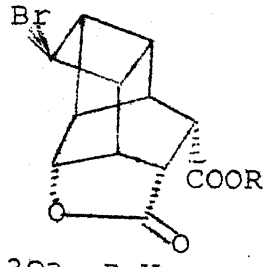


28

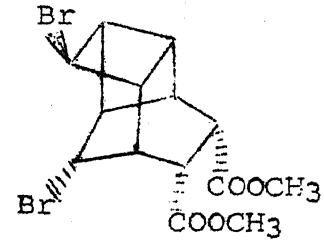
Nenitzescu[44] found that bromination of COT-maleic anhydride adduct (29) gave a bromolactone and assigned it the structure 30a. It was also observed that addition of bromine to diester 27 furnished a dibromoester and this was formulated as the tetracyclic compound 31. Simultaneously, Cookson[45] at Southampton, while working on the configuration of COT-maleic anhydride



29



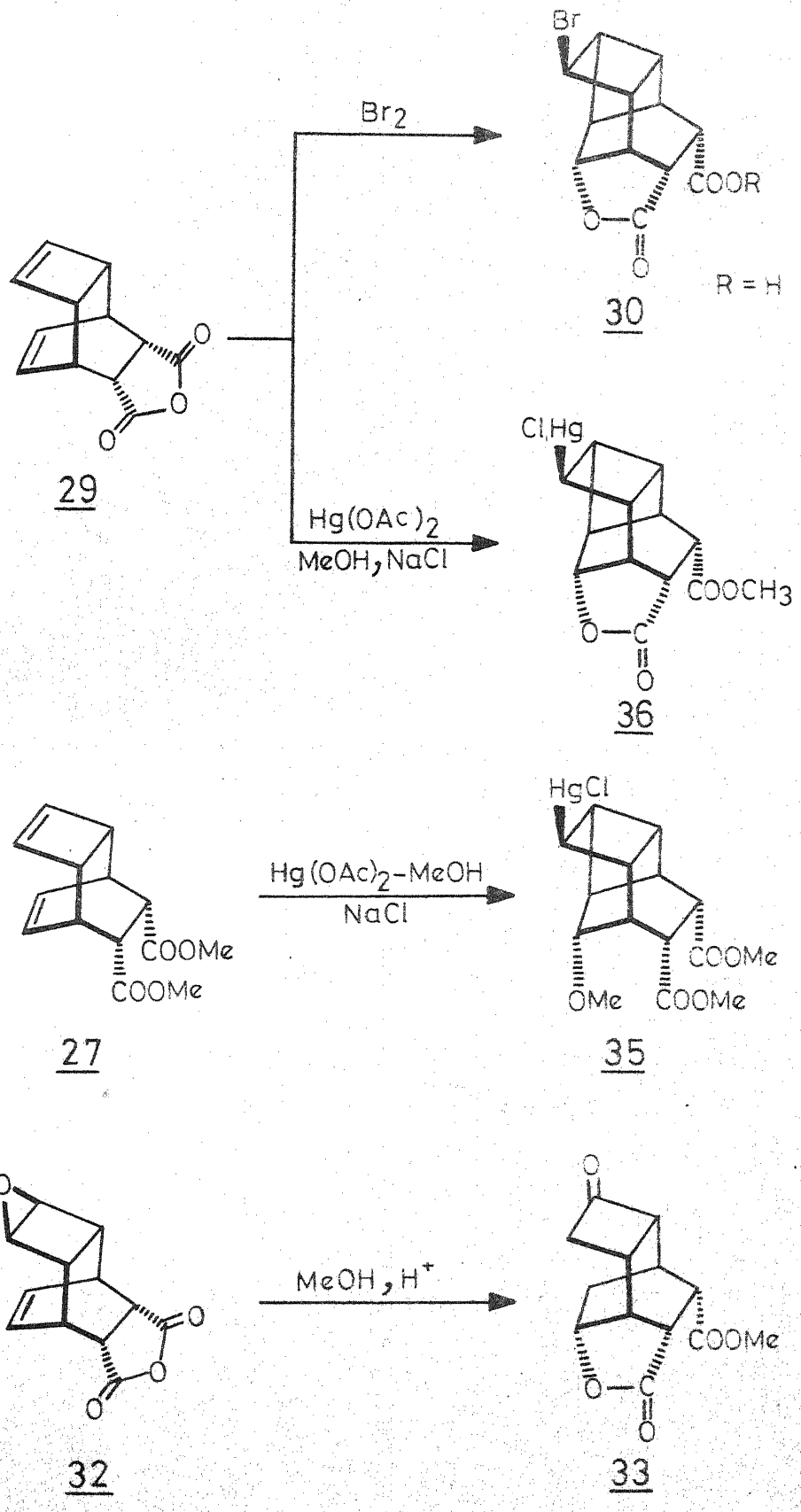
30a, R=H



31

adduct (29) studied a few electrophilic additions to this system and the results are described in Scheme II.11. Cookson confirmed[45] the formation of bromolactone (30a) from 29 during bromine addition. Epoxidation of 29 with peracid furnished the corresponding epoxide (32), which in acidic methanol rearranged to cyclobutanone (33) and hydroxylactone (34). Furthermore, methoxymercuration of both 27 & 29 was shown to proceed with transannular participation and the resulting mercurials were assigned structures 35 & 36, respectively.[45] It has been already shown[46] in the first chapter of this thesis that these structural assignments are incorrect. More recently, Farnum and Snyder[47] studied the competitive addition of bromine to several tricyclo [4.2.2.$0^{2,5}$] deca-3,7-diene derivatives but did not assign any firm structure to the

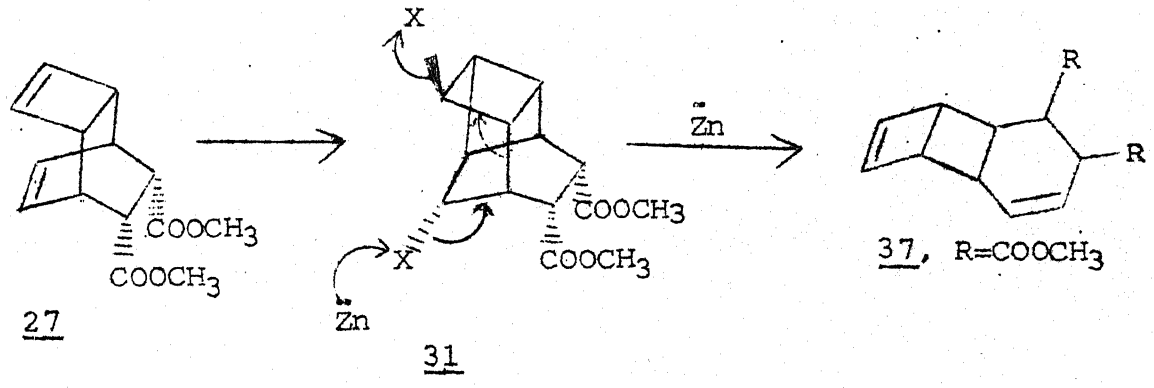
Scheme II.11


Br
Br2
COOR
R = H
30
29
Cl Hg
Hg(OAc)2
MeOH, NaCl
COOCH3
36
HgCl
Hg(OAc)2-MeOH
NaCl
COOMe
COOMe
OMe
COOMe
27
35
MeOH, H+
OH
COOMe
32
33
34

cyclised products. After the completion[48] of present investigation, Sasaki and coworkers[49] have reported the addition of some electrophiles to tricyclo [4.2.2.$o^{2,5}$] deca-3,7-diene system. However, some of their findings differ from ours and seem to be in error. It may be pointed out here that unlike the electrophilic additions, the photocyclisation of tricyclo [4.2.2.$o^{2,5}$] deca-3,7-diene system to basketane derivatives has been extensively studied[50-52] and is of great synthetic utility.[53,54]

We became interested in the exploitation of caged dibromide[44] like 31 for some novel and interesting transformations of synthetic value. Such a possibility, utilising the COT adduct (27) and leading to Dewarbenzene derivative 37 via a Grob-type[55] internal 1,4-elimination is depicted in Scheme II.12. As a prelude to such a transformation, the reaction of readily available[42] 9,10-dicarbomethoxytricyclo-[4.2.2.$o^{2,5}$] deca-3,7-diene (27) with halogens, pseudo halogens and peracid has been investigated. It has been observed

Scheme II.12



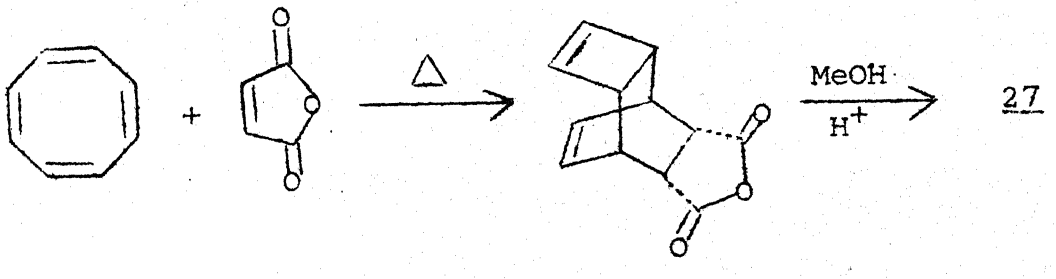
27 31 37, R=COOCH3

that addition of electrophiles to 27 proceeds *via* a novel cross-type cyclisation, contrary to that reported by Nenitzescu[44] and Cookson,[45] to furnish tetracyclic products of the type 25 and appears to be a general mode of cyclisation of this ring system.[48,49] Results of acid catalysed rearrangement of the epoxide 45 are also described in this chapter.

II.3 RESULTS AND DISCUSSION

As already mentioned, bromine, pyridinium hydrobromide perbromide,[56] iodobenzene dichloride,[57] iodine monochloride[58] and iodine nitrate[59] were selected as coreactant electrophiles for 9,10-dicarbomethoxytricyclo [4.2.2.$0^{2,5}$] deca-3,7-diene (27). The tricyclic diester (27) was readily obtained from COT *via* the standard reaction sequence[42] shown in Scheme II.13:

Scheme II.13



23 29

Reaction of 27 with bromine in the presence of UV irradiation, according to the procedure of Reppe,[42] furnished two products in a ratio of 5:1. These could be readily separated by column chromatography on a silica gel column. The major product, mp 179°, was easily identified as the bromolactone (ir: 1745, ester and 1765 cm^{-1}, γ-lactone, Fig. II.1), obtained earlier.[42,44] However, a careful and critical examination of its pmr spectral data (Fig. II.2 and Table II.1), in conjunction with other halolactones derived from 27 (see, Table II.1), revealed a major discrepancy with the purported structure. The gross pmr signals (100 MHz) of the bromolactone were in complete agreement with its formulation as either 30b or 38 but the appearance of endo-proton (H_a) attached to bromine as a sharp singlet (δ 3.85) was untenable with its formulation as 30b. An examination of molecular models indicated a nearly 90° dihedral angle between H_a and the vicinal methine protons in 38. On the other hand, the dihedral angle between H_a and vicinal methine protons showed substantial deviation (larger) from 90° in case of 30b and therefore H_a signal was expected to exhibit either some broadening or multiplicity. The sharp singlet due to H_a was conspicuously present in all the compounds reported in Table II.1. Furthermore, irradiation of pmr signal at δ 4.81 in 38 produced no perceptible change in the signal of the H_a proton. On the basis of structure 30b for the bromolactone, some coupling between H_a & H_b would have been certainly expected. Thus, structure 38

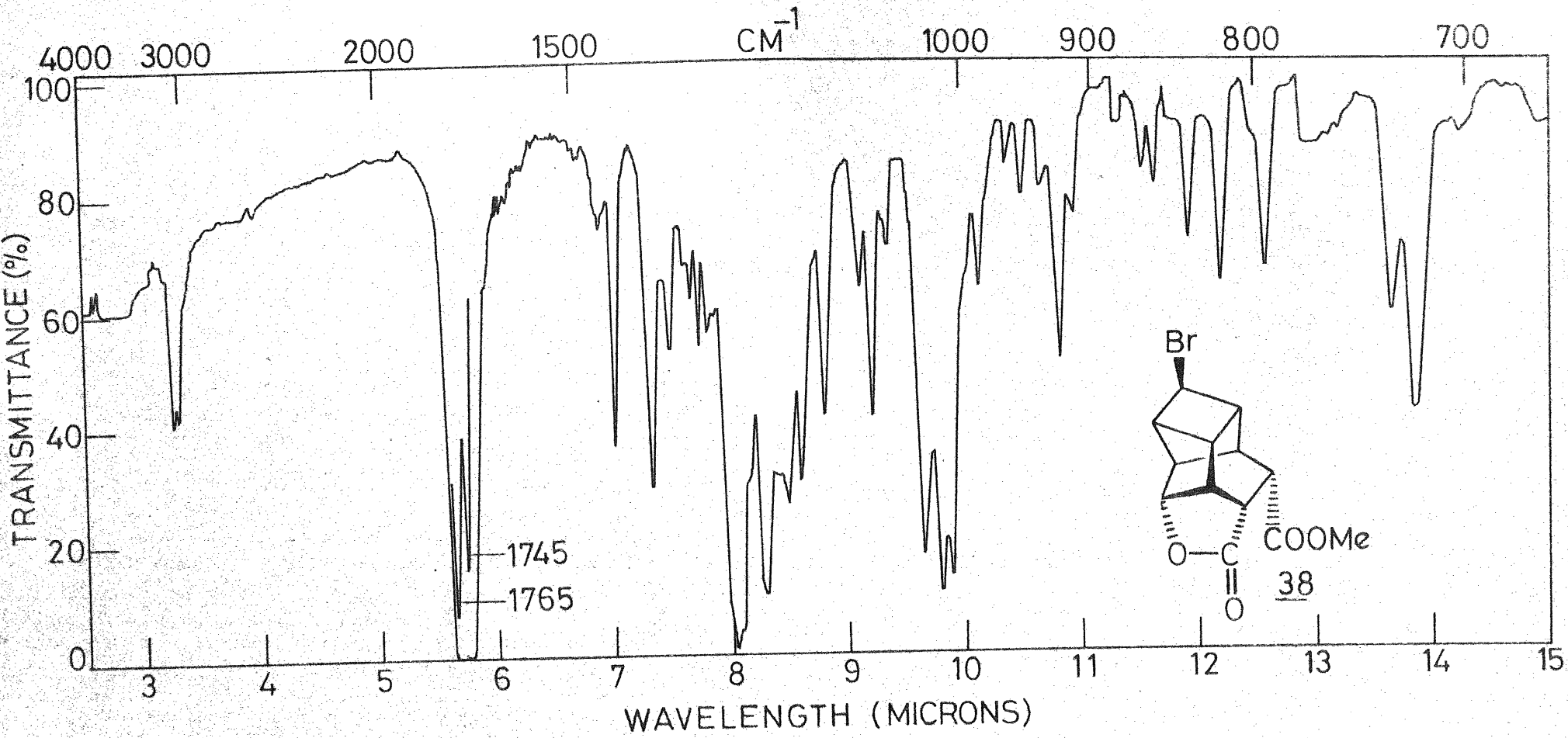


Fig. II.1 IR spectrum (KBr) of 38

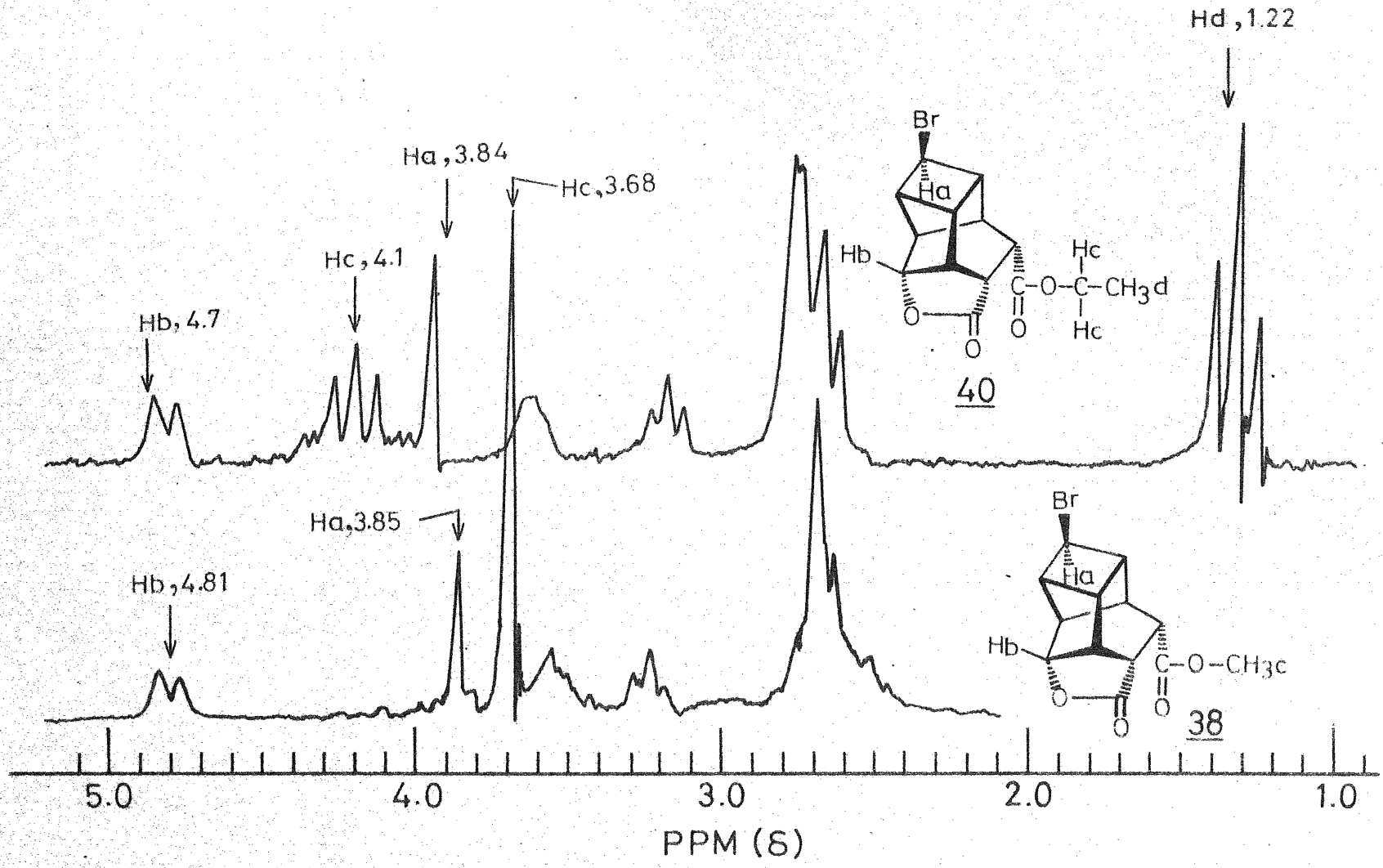


Fig. II.2 PMR spectrum (100 MHz) of 38 & 40

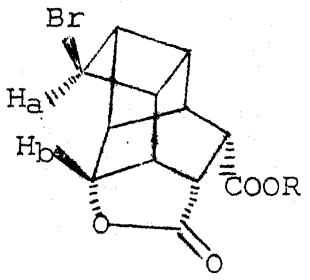
Table II.1

Compound	Electrophilic reagent	Product(s)	mp & yield	PMR spectral data
27	Br_2 (hν)	38	179°, 60%	4.81 (H-C-O-C=O, 1H, d),
27	$C_6H_5N^+HBr_3^-$	38	179°, 95%	3.85 (H-C-Br, 1H, s),
				3.68 (CH_3-O-C=O, 3H, s),
				3.6-2.5 (ring C-H, 8H, en)
27	$C_6H_5I^+Cl_2^-$	43	183°, 90%	4.86 (H-C-O-C=O, 1H, d),
				3.97 (H-C-Cl, 1H, s),
				3.73 (CH_3-O-C=O, 3H, s),
				3.6-2.5 (ring C-H, 8H, en)
27	ICl	44	161-2°, 87%	4.83 (H-C-O-C=O, 1H, d),
27	INO_3	44	161-2°, 80%	3.60 (H-C-I, 1H, s),
				3.67 (CH_3-O-C=O, 3H, s),
				3.55-2.5 (ring C-H, 8H, en)
42	EtOH-H^+	40	104°, -	4.7 (H-C-O-, 1H, d),
				4.1 ($-CH_2$-O-, 2H, t),
				3.84 (H-C-Br, 1H, s),
				1.22 (CH_3-CH_2, 3H, t).

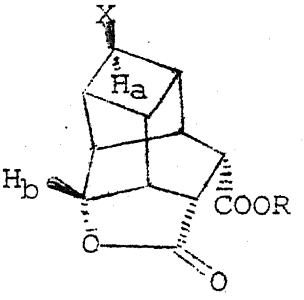
Table II.1 (contd.)

Compound	Electrophilic reagent	Product(s)	mp & yield	PMR spectral data
27	$m\text{-}ClC_6H_4CO_3H$	45	84-5°, 90%	6.32 (olefinic, 2H, t), 3.61 ($\underline{CH_3}$-O-C=O, 6H, s), 3.55 (, 2H, t), 3.4-2.27 (ring C-H, 6H, en)
45	BF_3-etherate	46	168-9°, 70%	4.7 (, 1H, d), 4.02 (, 1H, s), 3.62 ($\underline{CH_3}$-O-C=O, 3H, s), 3.54-2.18 (ring C-H and O-H, 8H, en)
45	$MeOH\text{-}H_2SO_4$	46	168-9°, 95%	
46	$C_6H_5N^+HCl^-CrO_3$	47	118-20°, 85%	4.81 ( , 1H, d), 3.66 ($\underline{CH_3}$-O-C=O, 3H, s), 3.5-2.5 (ring C-H, 8H, en).

derived via cross-type cyclisation is preferred to 30b for the bromolactone. This type of cyclisation seems to be quite



30b, $R=CH_3$



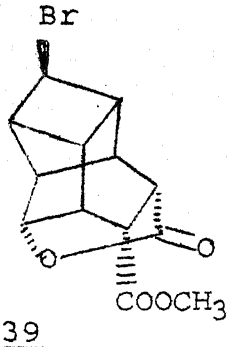
38, X=Br, $R=CH_3$
40, X=Br, $R=C_2H_5$
41, X=Br, R=H
43, X=Cl, $R=CH_3$
44 X=I, $R=CH_3$

general and the structural assignment is further supported by the results (vide infra) of acid catalysed rearrangement of epoxide (45). Another possible structure 39 for the bromolactone can be ruled out on the basis of ir stretching frequency (1765 cm^{-1}) of the lactone carbonyl in several halolactones of this series which is compatible[60] with a γ-lactone structure 38 rather than a δ-lactone structure 39.

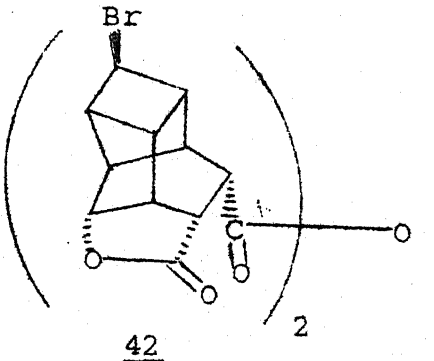
As expected, an attempted fragmentation of the bromolactone (38) with zinc in refluxing DMF did not succeed due to the unfavourable geometry (cf. the requisite geometry in 30b) and the unchanged starting material was recovered.

The minor product of Br_2 addition, mp 228°, was a highly insoluble material & showed an unusual absorption in its ir spectrum at 1850 cm^{-1} (anhydride?) along with the lactone bands at 1785 and 1765 cm^{-1}. Deu to its insolubility in most organic solvents, a satisfactory pmr spectrum for it could not be

obtained. However, the compound on treatment with methanol or ethanol in the presence of an acid furnished the corresponding methyl ester (38) or the ethyl ester (40, Fig. II.2) along with the bromolactone carboxylic acid (41). In view of this behaviour, the minor constituent is tentatively recognised as the anhydride (42). This product may be identical with the dibromide, mp 227°, obtained by Reppe[42] and Nenitzescu[44] to which they assigned structure 31. In our hands, we failed to obtain any material consonant with structure 31 during the bromination of 27.



39



42

Bromination of diester (27) with pyridinium hydrobromide perbromide[56] proceeded cleanly to furnish bromolactone 38 as the exclusive product in high yield. Addition of iodobenzene dichloride[57] and iodine monochloride[58] to (27) proceeded smoothly to yield the corresponding chloro and iodolactones (43) & (44) respectively (Table II.1). The structures of lactones 43 & 44 follow from analyses, infrared (Fig. II.3 & II.4) and particularly pmr spectra (Fig. II.5 & II.6). The pmr spectra of both 43 & 44 showed characteristic singlet resonances due to the proton attached to the halogen

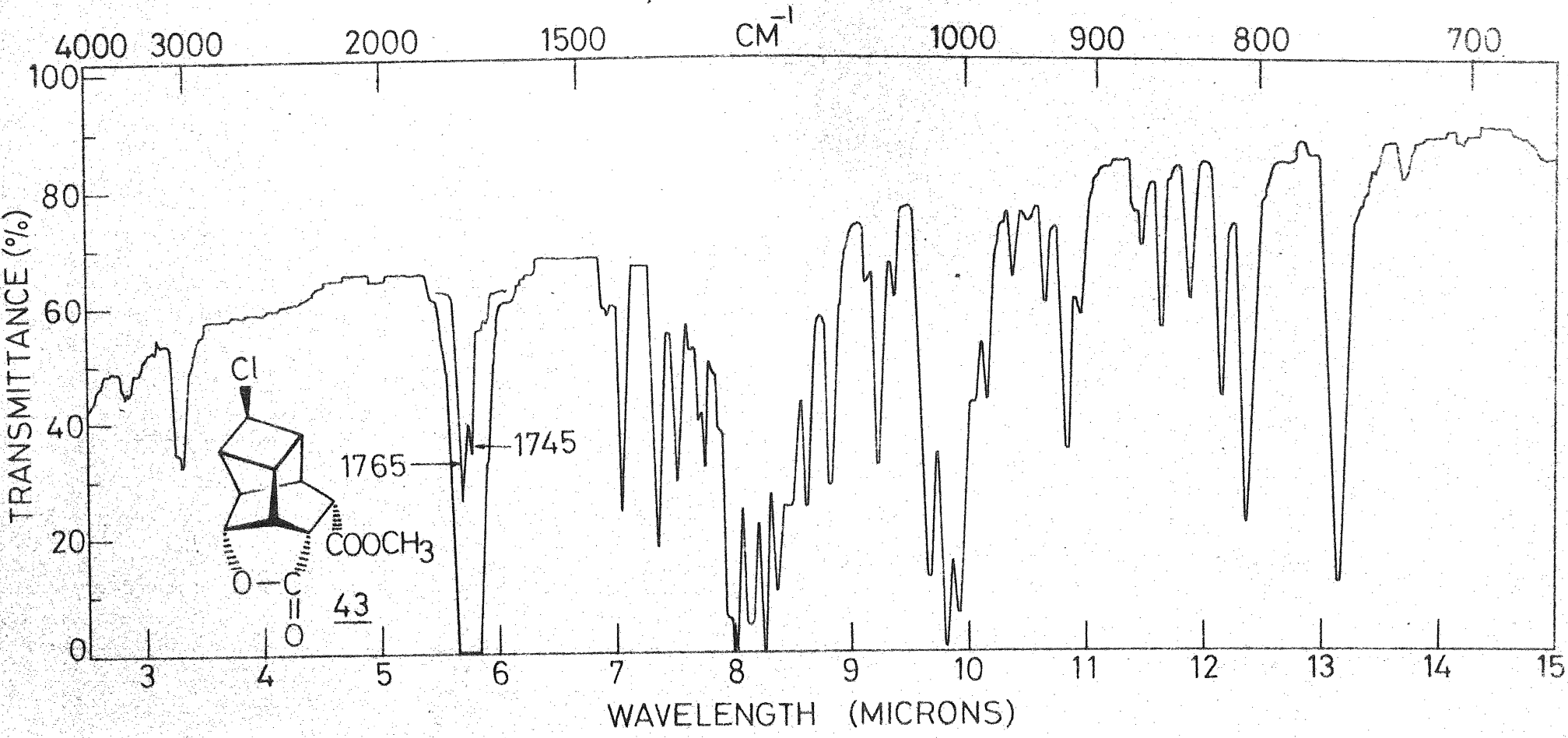


Fig. II.3 IR spectrum (KBr) of 43

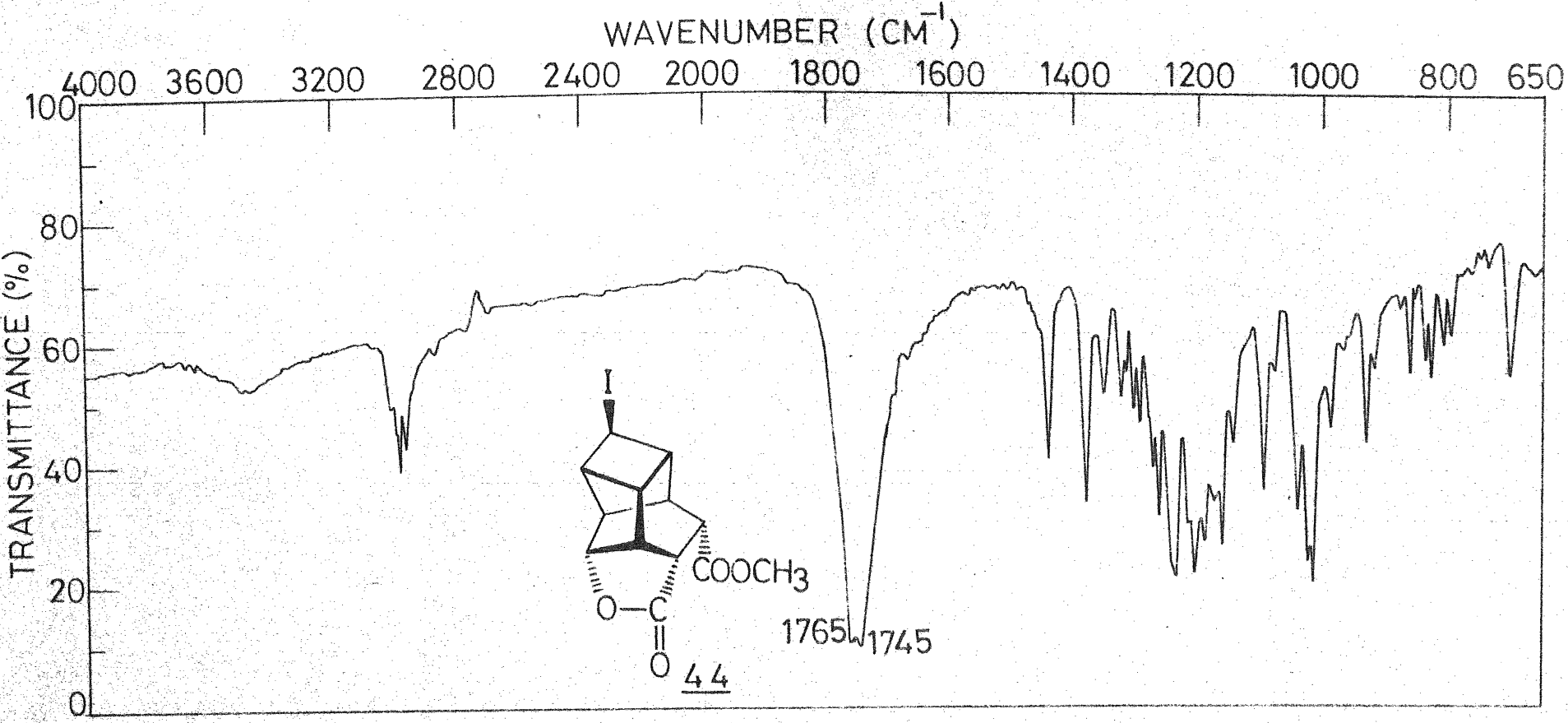
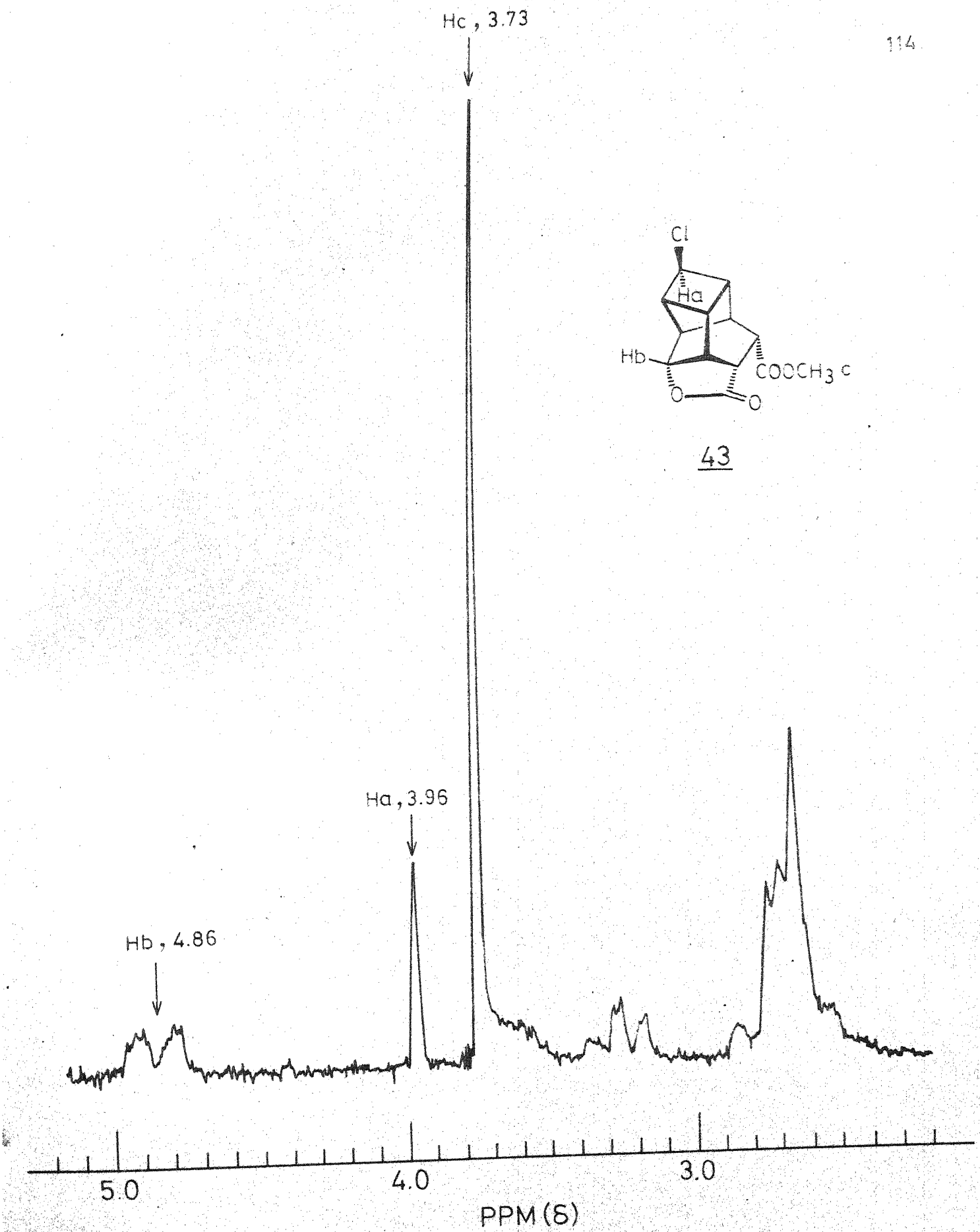
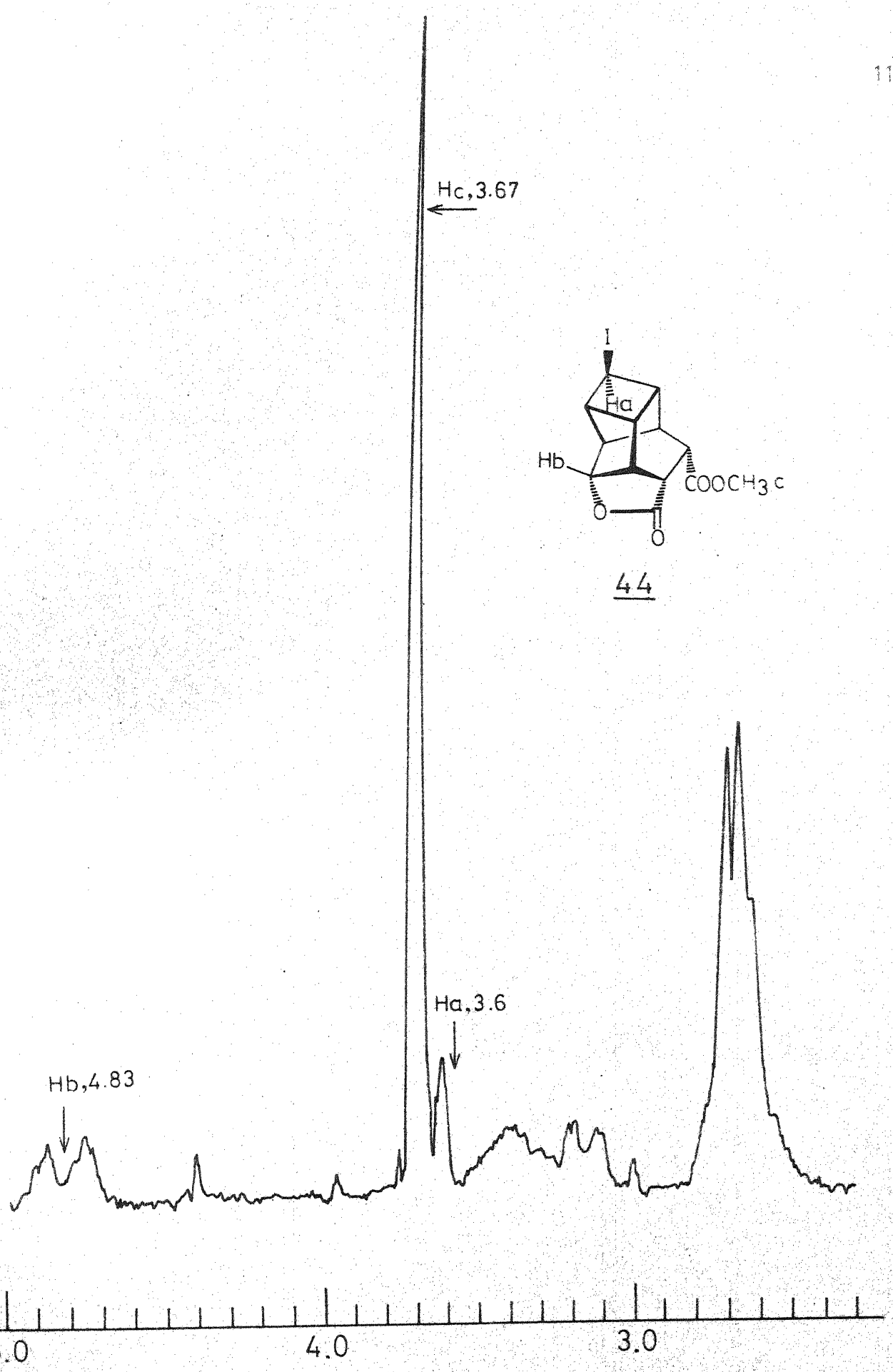


Fig. II. 4 IR spectrum (KBr) of 44



43

Fig. II.5 PMR spectrum (100 MHz) of 43

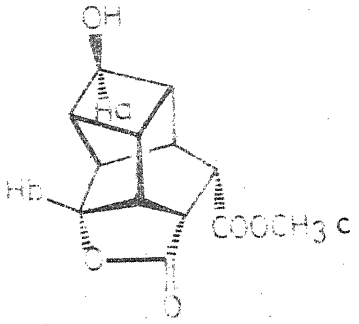


44

Fig.II.6 PMR spectrum (100MHz) of 44

atom at δ 3.96 & δ 3.60 respectively. The other pmr characteristics are in conformity with their structures (Table II.1). Similarly, reaction of iodine nitrate[59] with 27 furnished only the iodolactone (44) in high yield.

Addition of m-chloroperbenzoic acid to 27 proceeded readily to furnish a monoepoxide (45), mp 84°. The structure of 45 follows from its pmr spectrum that showed a 2H triplet at δ 6.32 for the olefinic protons along with another 2H triplet at δ 3.55 (J=2Hz) for the protons attached[61] to the oxirane ring. Rearrangement of the epoxide (45) with BF_3-etherate under forcing conditions gave a tetracyclic alcohol (46), mp 168-9°, in poor yield. However, better yields of this rearranged alcohol could be realised by carrying out the rearrangement in methanol-sulphuric acid mixture. This alcohol must be identical with compound 34 obtained earlier by Cookson (Scheme II.11). The pmr spectrum of 46 (Fig. II.7) was devoid of any olefinic proton absorption which was indicative of transannular participation by the C_7-C_8 double bond. It exhibited characteristic 1H singlet at δ 4.02 due to the endo-proton attached to the hydroxyl along with a doublet at δ 4.7 due to the proton attached to carbon bearing the lactonic oxygen. The other pmr features were in accordance with the expected structure 46. Oxidation of 46 with pyridinium chlorochromate afforded the tetracyclic ketone 47 which exhibited the resonance due to H_b at δ 4.81 (cf. H_b resonance



46

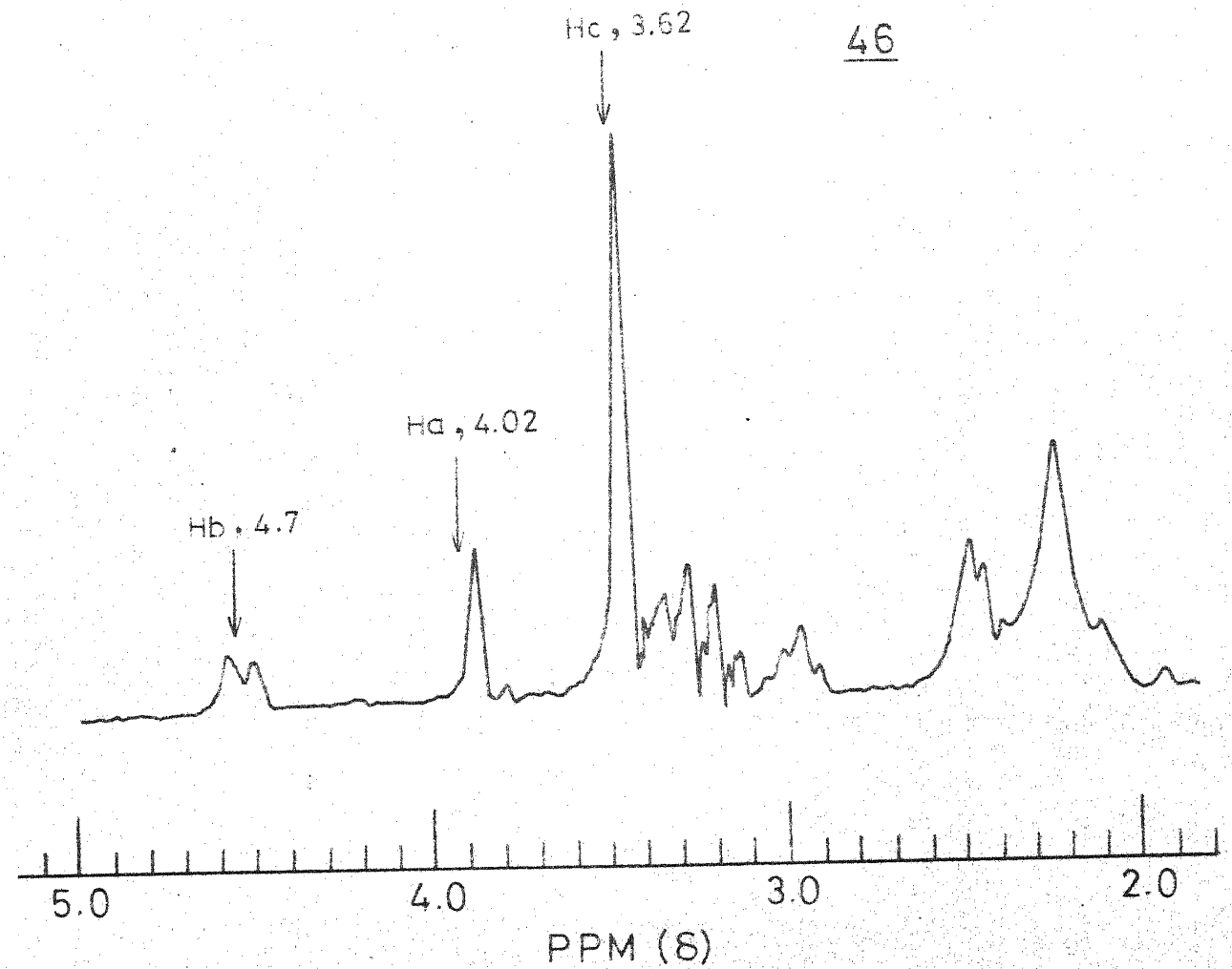
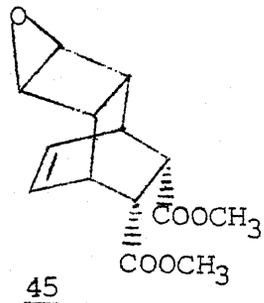
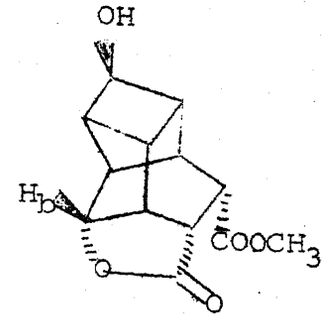


Fig. II.7 PMR spectrum (100 MHz) of 46

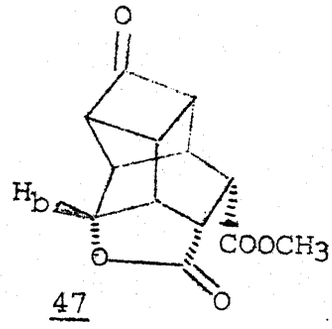
at δ 4.7 in the precursor alcohol 46). This insignificant alteration in the H_b resonance in going from alcohol(46)to cyclobutanone(47)provides strong support for its structure arising from a cross-type cyclisation. Alternate formulation 48 for the rearranged ketone would have definitely required a significant perturbation in H_b chemical shift due to its proximate geometrical relationship with the carbonyl group. The rearrangement product of epoxide (45) is thus formulated as 46 instead of 34, assigned earlier by Cookson[45] to one of the rearrangement products of the epoxide (32) with acidic methanol.



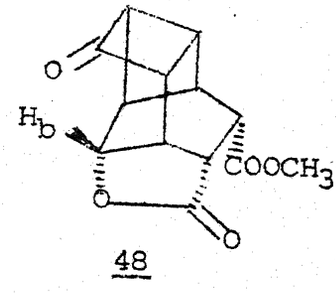
45



46



47



48

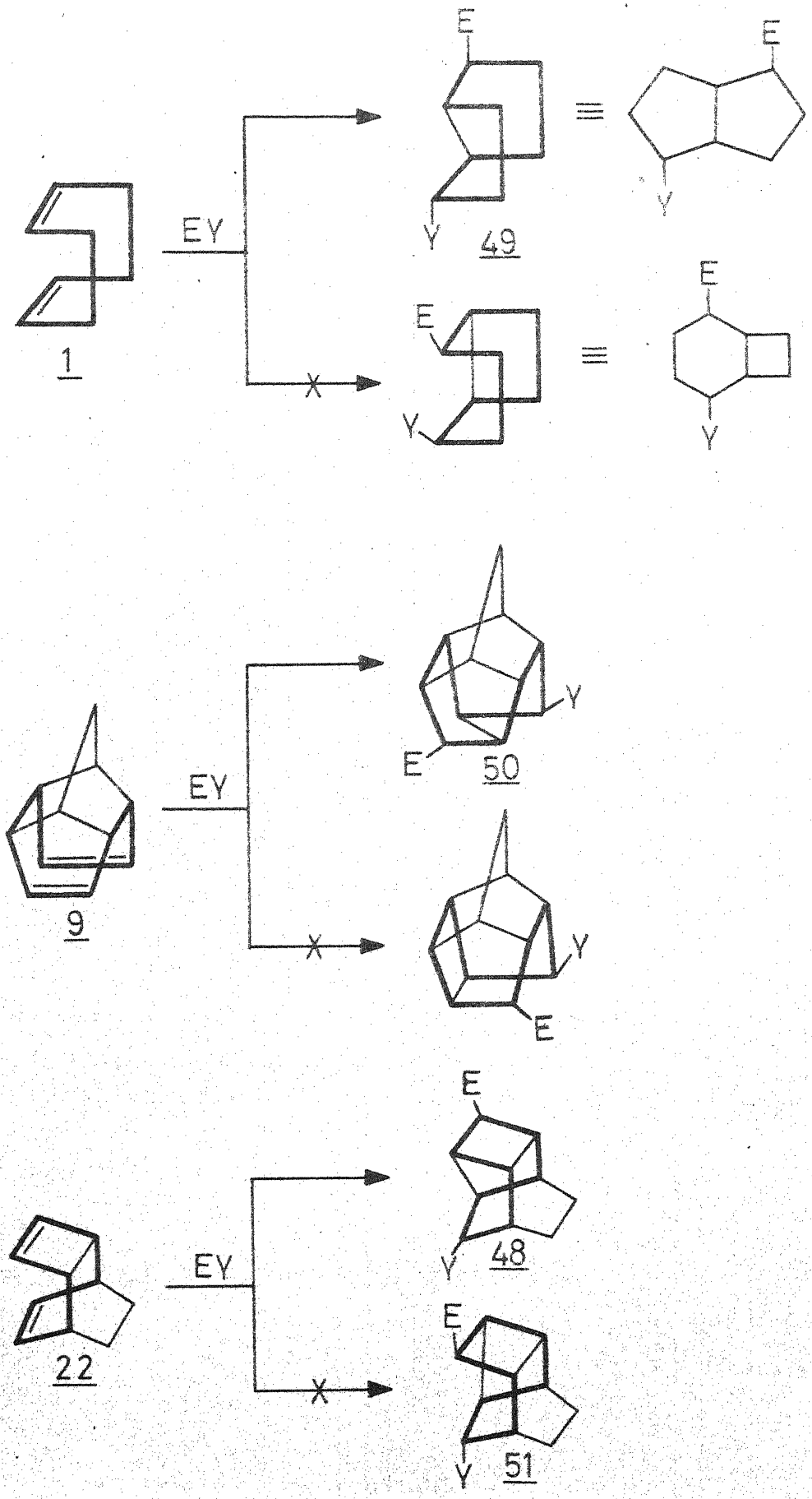
The novel cross-type of cyclisation of tricyclo deca-3,7-diene ring system (22) to 49 observed here is in analogy with the usually encountered transannular cyclisations of

1,5-cyclooctadiene[15-21] (1) and polycyclic olefin[10] (9). In fact, both 22 & 9 can be formally considered as bridged 1,5-cyclooctadiene derivatives (heavy lines in 22 & 9, Scheme II.14) and thus expected to follow the cyclisation pattern of parent 1 (Scheme II.14). It is noteworthy that cyclisation of 1 to 50 or of 9 to 51 has not been encountered during extensive study of electrophilic additions to these systems. An inspection of stereomodels suggests that the driving force for this preferential cross-type cyclisation of 22 is the release of torsional strain (staggering of cyclobutane methine hydrogens) in the formation of 49 as compared to formation of 52. In the light of results reported here, structures of various cyclisation products of diene system 22 reported in literature[42,45,47] must be appropriately revised.

II.4 EXPERIMENTAL SECTION

All melting points are uncorrected and were taken in capillaries on a Thomas-Hoover melting point apparatus. All solvent extracts were washed with brine and dried over anhydrous sodium sulphate. Infrared spectra were recorded on a Perkin-Elmer Model 137B and Perkin-Elmer 521 spectrophotometer as KBr discs. PMR traces were recorded on a Varian A-60D and HA-100 spectrometers using tetramethylsilane (TMS) as the internal standard. Chemical shifts are reported on δ scale. Microanalyses were performed by Mr. A.H. Siddiqui in Coleman-automatic carbon-hydrogen and nitrogen analysers.

Scheme II.14



9,10-Dicarbomethoxytricyclo[4.2.2.$o^{2,5}$]deca-3,7-diene (27)

This was prepared by the reaction of COT-maleic anhydride adduct with methanol in the presence of catalytic amounts of conc. H_2SO_4 as described in the literature.[42] Distillation and crystallisation from pet ether gave colourless crystals of diester 27, bp 130°/1.5 mm, mp 52-53°.

IR spectrum (KBr): 1745 and 1200 cm^{-1} (ester).

PMR spectrum (CCl_4): δ 5.75-5.95 (olefinic, 4H, m), 3.51 ($\underline{CH_3}$-O-$\overset{|}{C}$=O, 6H, s) and 2.65-2.95 (C-$\underline{H}$ ring, 6H, m).

Addition of bromine to 27

The above diester (1.0 g) in benzene (20 ml) was exposed to UV light (Hanovia 450 Watt lamp) and bromine (0.4 ml) was slowly added from a pipette. After 2 hr the solvent was removed and the residual solid charged on a solica gel (20 g) column. Elution with pet ether-benzene (30:70) gave 780 mg (60%) of a pure solid. Recrystallisation from benzene gave lovely white crystals of 38, mp 179° (lit.[45] mp 178-79°).

IR spectrum (KBr): 1765 (lactone and 1745 cm^{-1} (ester).

PMR spectrum ($CDCl_3$): δ 4.81 ($\underline{H}$-$\overset{|}{C}$-O-, 1H, d), 3.85 ($\underline{H}$-$\overset{|}{C}$-Br, 1H, s), 3.68 (CH_3-O-$\overset{|}{C}$=O, 3H, s), 3.6-2.5 (ring C-H, 8H, en).

Anal. for $C_{13}H_{13}O_4Br$ Calcd: C, 49.84; H, 4.18.

Found: C, 49.88; H, 4.28.

Further elution of the column with benzene-ethyl acetate (70:30) gave 150 mg (12%) of 42 as a white solid, mp 228°, ir spectrum: 1850 (anhydride), 1785 and 1765 cm^{-1} (lactone). The above solid (100 mg) was dissolved in ethanol (5 ml) and a drop of conc. H_2SO_4 added. The mixture was left aside for a few hr and the tlc (benzene-ethyl acetate, 50:50) showed two spots. Usual work-up gave a solid (85 mg) and was charged on a silica gel column. Elution with benzene gave 40 as a colourless crystalline solid, mp 104°.

IR spectrum (KBr): 1765 (lactone) and 1745 cm^{-1} (ester).

PMR spectrum ($CDCl_3$): δ 4.7 (H-C-O-, 1H, d), 4.1 ($-CH_2-O-$, 2H, t), 3.84 (H-C-Br, 1H, s), 1.22 (CH_3-CH_2-, 3H, t).

Further elution of the column with ethyl-acetate gave colourless crystals of 41, mp 236° (lit.[45] 238°), ir spectrum: 1760 and 1690 cm^{-1}. The structure of 41 was further confirmed by its conversion to 38 with methanol in the presence of an acid.

Reaction of pyridinium hydrobromide perbromide[56] with 27

The diester (0.5 g, 2 mmol) in acetic acid (10 ml) was mixed with pyridinium hydrobromide perbromide (0.65 g, 2 mmol) slowly and reaction mixture was stirred for two hr at room temperature till the reaction was complete (tlc). The reaction mixture was poured into water (25 ml) and extracted with

ether(20mlx3), washed with sodium bicarbonate solution. Removal of solvent yielded crystalline solid 38 (0.6 g, 95%). Recrystallisation from benzene gave nice white solid, mp 179°. This compound was identical with the bromolactone obtained on bromination of 27.

Addition of iodobenzene dichloride[57] to 27

To a stirred solution of ester (27, 0.5 g, 2 mmol) in chloroform (10 ml), iodobenzene dichloride (0.56 g, 2 mmol) was slowly added and the reaction mixture was stirred at room temperature for one hr. The reaction mixture was poured into water (10 ml), extracted with chloroform (10 ml x3), washed and dried. Removal of solvent yielded 43. Recrystallisation from benzene gave white crystals 0.49 g (90%), mp 183°.

IR spectrum: 1745 (ester), 1765 (lactone) and 1250 cm^{-1}.

PMR spectrum ($CDCl_3$): δ 4.86 (H-C-O-, 1H, d), 3.97 (H-C-Cl, s), 3.73 (CH_3-O-C=O, 3H, s), 3.6-2.5 (ring C-H, 8H, en).

Anal. for $C_{13}H_{13}O_4Cl$ Calcd: C, 58.1, H, 4.8.

Found: C, 58.43; H, 4.98.

Addition of iodine monochloride[58] to 27

Iodine monochloride(0.7 g, 4.3 mmol) was added slowly to a stirred solution of ester (27, 1 g, 4 mmol) in methanol (15 ml). The reaction mixture was stirred for 2 hr at room temperature, poured into water (20 ml) and extracted with methylene dichloride (20mlx 3)). Washing, drying and

removal of solvent yielded pale yellow residue 1.3 g (87%). Recrystallisation from methanol gave 44 as white flakes, mp 161-62°.

IR spectrum: 1765 (lactone), 1745 (ester) and 1245 cm^{-1}.

PMR spectrum ($CDCl_3$): δ 4.83 (H-C-O-C=O, 3.6 (H-C-I, 1H, s), 3.67 (CH_3-O-C=O, 3H, s), 3.55-2.5 (ring C-H, 8H, en).

Anal. for $C_{13}H_{13}O_4I$ Calcd: C, 43.30; H, 3.60.
Found: C, 43.74; H, 3.54.

Addition of iodine nitrate[59] to 27

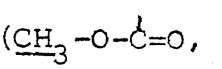
Silver nitrate (0.36 g, 2.1 mmol) and iodine (0.54 g, 4.2 mmol) in acetonitrile (10 ml) were stirred for 15 min. To this stirring reaction mixture, ester (27, 0.5 g, 2 mmol) was added and continued stirring for further 1 hr. The mixture was poured into water, extracted with methylene chloride (15 ml x 3), washed with sodium thiosulphate solution and finally with brine. Removal of solvent and crystallisation from methanol yielded 0.6 g (80%) of white crystals of 44, mp 161-62°. This product was identical in all respects with the iodolactone (44) obtained via addition of iodine monochloride to 27.

Reaction of m-chloroperbenzoic acid with 27

The diester (1 g, 4 mmol) in benzene (25 ml) was mixed with m-chloroperbenzoic acid (0.9 g, 80%) and left aside at

room temperature for 4 hr, till the reaction was complete (tlc). The reaction mixture was poured into aq. sodium bicarbonate solution and twice extracted with benzene (25 ml x 2). The combined benzene extracts were washed and dried. Removal of solvent gave 0.9 g of a solid residue. Recrystallisation from pet ether gave microcrystals of 45, mp 84-5°.

IR spectrum: 1745 (ester), 910 and 935 cm^{-1} (epoxide).

PMR spectrum ($CDCl_3$): δ6.32 (olefinic, 2H, t), 3.61 ($\underline{CH_3}$-O-C=O, 6H, s) and 3.55 ( , 2H, t).

Anal. for $C_{14}H_{16}O_5$ Calcd: C, 63.63; H, 6.06.
Found: C, 63.36; H, 6.18.

BF_3-Catalysed rearrangement of epoxide 45

The above epoxide (1 g) in methylene chloride (10 ml) and BF_3-etherate (0.2 ml) were mixed and left overnight at ambient temperature (38°C). The reaction mixture was poured into acueous sodium bicarbonate and extracted with methylene chloride (20 ml x 2). The combined organic extracts were washed, dried and freed of solvent to give (950 mg) of glassy reasidue. This material was absorbed on a silica gel column and eluted with benzene-ethyl acetate (80:20) to give tlc pure 46 (0.6 g, 70%) as a glassy solid, which on crystallisation from pet-ether benzene gave white needle shaped crystals, mp 168-69°.

IR spectrum: (thin film): 3550 (hydroxyl), 1765 (lactone), 1745 cm^{-1} (ester); (KBr): 3500 (hydroxyl), 1745 (broad peak), 1210 cm^{-1}.

PMR spectrum ($CDCl_3$): δ 4.7 (H-C-O-, 1H, d), 4.02 (H-C-OH, 1H, s), 3.62 (CH_3-O-C=O, 3H, s), 3.5-2.18 (ring C-H and -O-H, 9H, en).

Anal. for $C_{13}H_{14}O_5$ Calcd: C, 62.39; H, 5.83.
Found: C, 61.95; H, 5.83.

Acid catalysed rearrangement of epoxide 45

The epoxide (45, 0.2 g) in methanol (5 ml) and conc. H_2SO_4 (0.5 ml) were mixed and kept at room temperature for 1 hr. The reaction mixture was poured into water (10 ml) and extracted with methylene chloride (15 ml x 2), washed with aqueous sodium carbonate and dried. Removal of solvent yielded 0.19 g (95%) of 46, which on crystallisation from benzene gave white needle shaped crystals, mp 168-69°. This compound was identical with 46 described in the above experiment.

Oxidation of alcohol (46) with pyridinium chlorochromate[62]

To a suspension of pyridinium chlorochromate (0.25 g, 0.11 mmol) in methylene chloride (5 ml) was added a CH_2Cl_2 solution of alcohol (46, 0.15 g, 0.06 mmol). The reaction mixture was stirred for 2 hr at room temperature; diluted with ether (10 ml) and then directly filtered through a small silica gel column to yield 0.12 g (80%) of crude ketone (47). Crystallisation from pet ether-benzene furnished colourless crystals of 47, mp 118-20°.

IR spectrum (KBr): 1800-1765 (broad band, cyclobutanone and lactone carbonyl), 1745 cm^{-1} (ester).

PMR spectrum ($CDCl_3$): δ4.81 ($\underline{H}$-C-O-C=O, 1H, d), 3.66 ($\underline{CH_3}$-O-C=O, 3H, s), 3.5-2.5 (ring C-H, 8H, en).

Reaction of bromolactone (38) with zinc in dimethylformamide

The bromolactone (38, 0.1 g) and zinc dust(35 mg) in DMF (5 ml) were heated at 110° for 3 hr. The mixture was poured into water and extracted with ethyl acetate (15mlx 2). The organic extract was washed and evaporated to a solid residue. This residue was identified (tlc, IR) as the starting material.

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CHAPTER III

A FASCINATING 1,3-BISHOMOCUBANE $\longrightarrow$ BRENDANE REARRANGEMENT

III.1 ABSTRACT

A novel one step rearrangement of pentacyclo-[5,3.0.$0^{2,5}$.$0^{3,9}$.$0^{4,8}$]decan-6-one (1,3-bishomocubanone, 27) to 2,9-disubstituted tricyclo[4.2.1.$0^{3,7}$]non-4-ene (brend-4-ene, 40) is reported. Reaction of 1,3-bishomocubanone (27) with sodium azide in methanesulphonic acid furnished a crystalline mesylate 30 as the major product of the reaction. The structure of exo-2-methanesulphonoxy-9-cyanobrend-4-ene (30) has been delineated on the basis of spectroscopic data and chemical transformations. Brief exposure of 30 to base led to a facile 1,3-elimination and 2-cyanodeltacyclene (41) was obtained. The deltacyclene derivative 41 underwent a facile acetone sensitised photochemical $\sigma^2s + \pi^2s$ addition to 2-cyanopentacyclo[4.3.0.$0^{2,4}$.$0^{3,8}$.$0^{5,7}$]nonane (norsnoutane, 45).

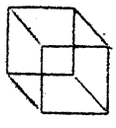
These reactions elucidate the carbocyclic skeleton present in 30 and also establish the location of the functional groups. A plausible mechanism is proposed for the 1,3-bishomocubanone (27) $\rightarrow$ brend-4-ene (30) transformation. The results and discussion are preceded by a brief, schematic review of transformations of cubane and congeners.

III.2 INTRODUCTION

Molecular design and rearrangements of strained polycyclic compounds have been areas of intense activity and sustained fascination in recent years.[1-7] This high level of interest has been fostered by the numerous unique transformations of small rings that have been unravelled and by the intrinsic desire of organic chemists to understand strain — reactivity relationships. In particular, efforts have been focussed on the study of solvolytic behaviour and transition metal catalysed rearrangements[8] to gain insight into the nature of the transition states, reactive intermediates and strain release factors in carbonium ion rearrangements.

Among the various types of small strained carbocycles, those belonging to the cubane "cage" family are of special interest on several counts. For many years, investigation of these interesting systems was hampered due to the formidable synthetic challange associated with the construction of these molecules. However, with the discovery and efficient use of

intramolecular $\pi^2s + \pi^2s$ photoadditions[9,10] for the construction of "caged" space-enclosing systems, it has been possible to produce[11-21] various compounds of cubane family in quantities sufficient for further chemical exploration. Besides cubane (1), other members of this family whose frameworks have been synthesised[11-21] and chemistry explored are homocubane (2), secocubane (3), 1,1-bishomocubane (4), 1,2-bishomocubane (5), 1,3-bishomocubane (6), 1,3'-bishomocubane (7) and



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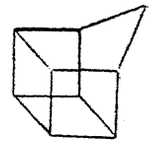

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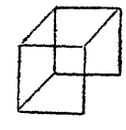

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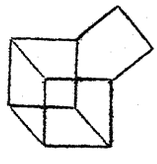

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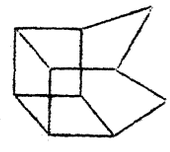

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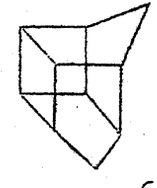

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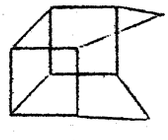

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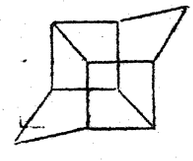

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1,4-bishomocubane (8).≠

The reactions of cubyl systems (1 - 8) can be conveniently discussed under three main categories. These are transition metal catalysed valence isomerisations, solvolytic rearrangements *via* carbonium ions and miscellaneous transformations. A brief discussion of these rearrangements is presented here. Most of the reactions are depicted in simple flow chart format.

TRANSITION METAL CATALYSED REARRANGEMENTS

Highly strained polycyclic cyclobutane compounds (cubane type), particularly those incorporating a fused bicyclo[2.2.0]-

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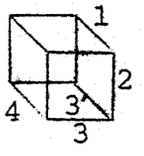
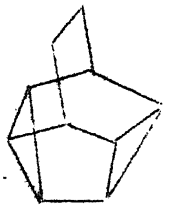
≠ The numbering for the bishomocubane system of nomenclature refers to the shortest path along the edges of a cube between the position of two methylene bridges. Thus the five possible bishomocubanes are as follows: pentacyclo[4.4.0.$0^{2,5}$.$0^{3,8}$.$0^{4,7}$]-decane, 1,1-bishomocubane (4); pentacyclo[4.4.0.$0^{2,5}$.$0^{3,9}$.$0^{4,7}$]-decane, 1,2-bishomocubane (5); pentacyclo[5.3.0.$0^{2,5}$.$0^{3,9}$.$0^{4,8}$]-decane, 1,3-bishomocubane (6); pentacyclo[4.4.0.$0^{2,5}$.$0^{3,9}$.$0^{4,8}$]-decane, 1,3'-bishomocubane (7); pentacyclo[5.3.0.$0^{2,6}$.$0^{3,9}$.$0^{4,8}$]-decane, 1,4-bishomocubane (8).



hexane moiety are so constructed that they are capable of rapid and quantitative bond reorganisation in presence of transition metal ions.[8] So facile are these rearrangements, that the first such process discovered accidentally in 1965 by Furstoss and Lehn[22] remained undetected for the next five years. These authors synthesised several 1,1-bishomocubane derivatives 4 and purified their products through silver nitrate impregnated silica gel chromatography. The passage of 1,1-bishomocubanes through the silver column rearranged all the compounds to snoutane (9) derivatives as was shown later by Dauben[23] in 1970. This observation triggered off a flurry of activity in the area of transition metal catalysed rearrangements of cubyl systems.[5,6,24-28]

The bond reorganisations generally encountered in the cubyl framework are of two extreme types. The first type is promoted by Ag(I) ($4d^{10}$) and related metal ions having substantial σ electron acceptor ability which results in thermodynamically favourable dicyclobutane $\rightarrow$ dicyclopropane bond switching. This is in essence a transformation of four cyclobutane rings into two cyclopropane and two cyclopentane rings and is exemplified by the 1,1-bishomocubane (4) $\rightarrow$ snoutane (9) rearrangement. Paquette[29] and Dauben[23] have independently investigated these reactions and shown that cubane (1) rearranges to cuneane (10) and homocubane (2) to norsnoutane(11). The bond reorganisation involved in these rearrangements is formally a symmetry disallowed $\sigma^2a + \sigma^2a$ change which results

in concomitant expansion and contraction of two four membered rings.



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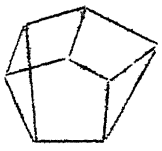

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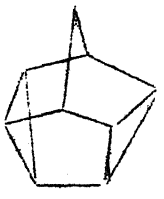

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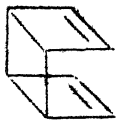

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The second type of process induced by transition metals such as Rh(I) ($4d^8$), with decided capacity for oxidative addition, results in cyclobutane $\rightarrow$diolefin type rearrangement. This process is formally a reversal of photochemically induced $\pi^2s + \pi^2s$ cage cyclisation. Rhodium(I) catalysed cubane (I) to <u>syn</u>-tricyclo$\left[4.2.0.0^{2,5}\right]$octa-3,7-diene (12) change[30,31] is a typical example of this process. In Scheme III.1 are summarised various transition metal catalysed valence isomerisations of cubyl systems. Several examples of substituted derivatives[24-28] have also been incorporated to highlight regio- and stereospecificity of these reactions. The relative simplicity of these transformations and high yields generally encountered have culminated in the synthesis of novel and here-to-fore elusive molecules.

Scheme III.1

CUBANES AND SECOCUBANE

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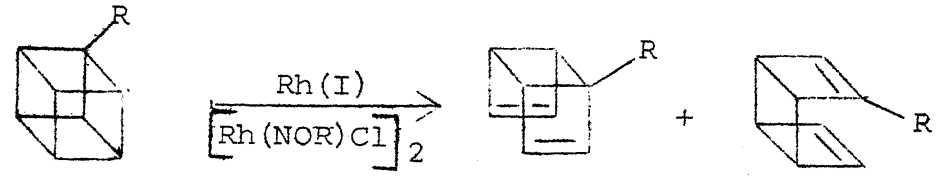

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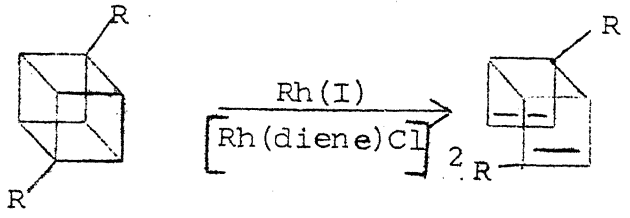

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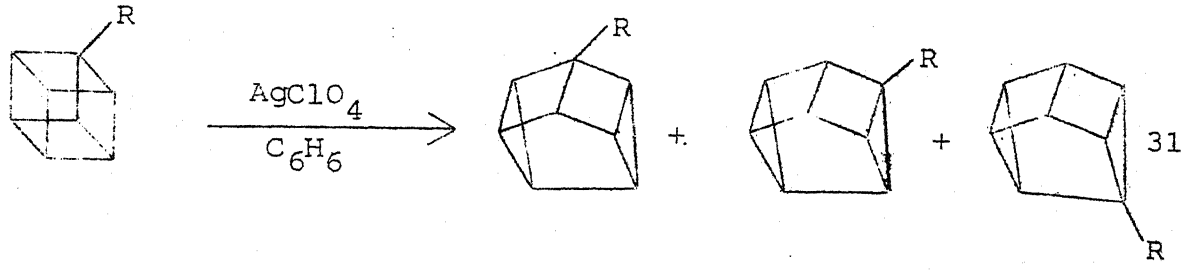

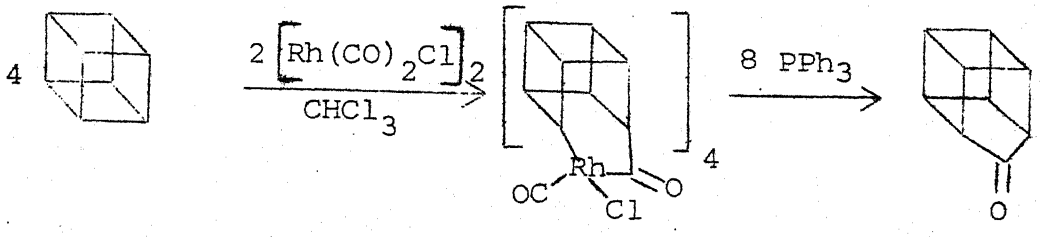

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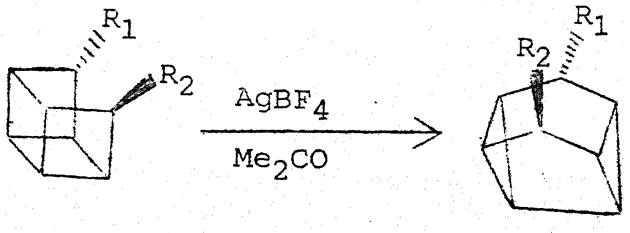

32,33

Scheme III.1 (contd.)

HOMOCUBANES

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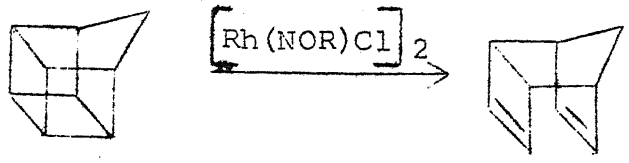

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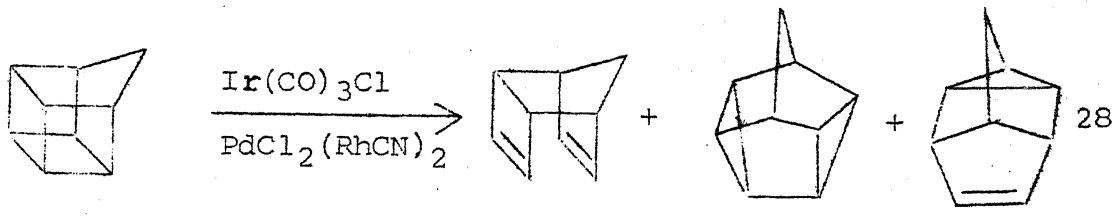

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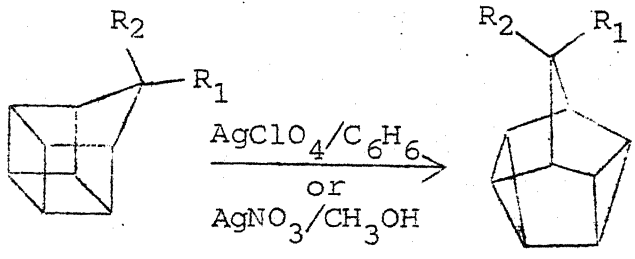

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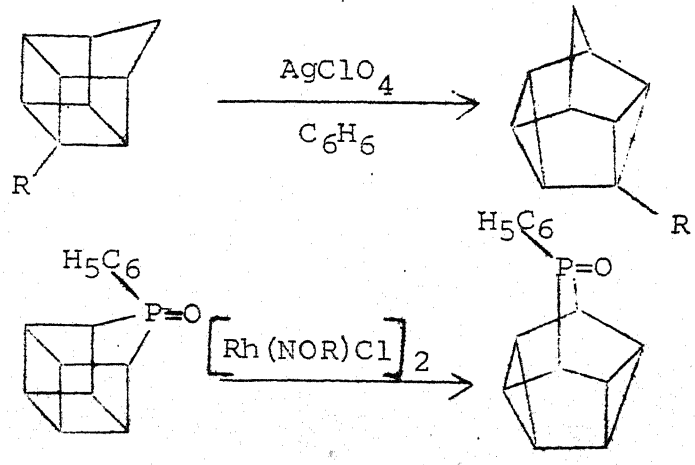

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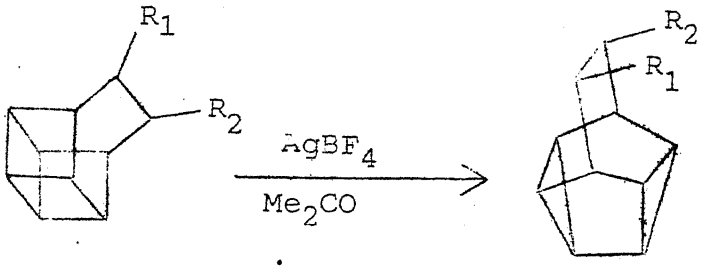
34

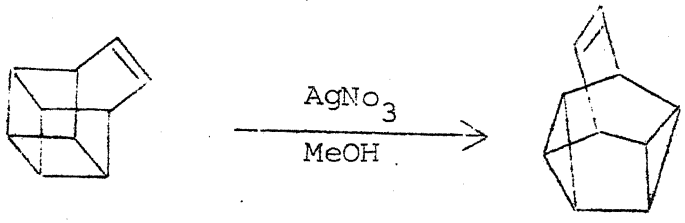
Scheme III.1 (contd.)

1,1-BISHOMOCUBANES

Ref.



24,25, 33



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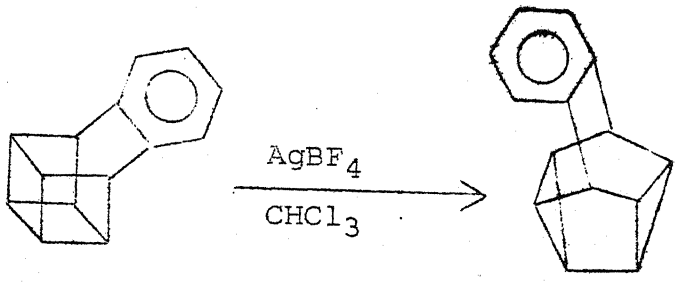

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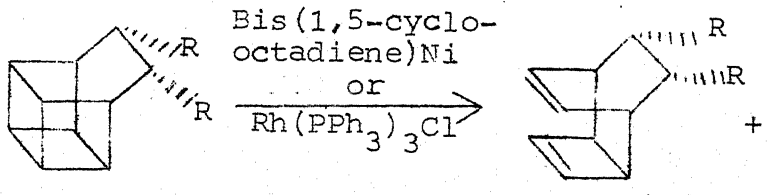
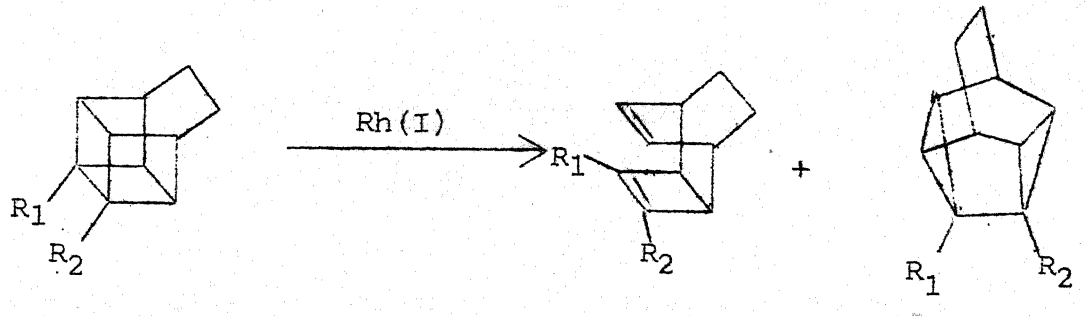


36,37

R= $COOCH_3$ R= $COOCH_3$ R= $COOCH_3$



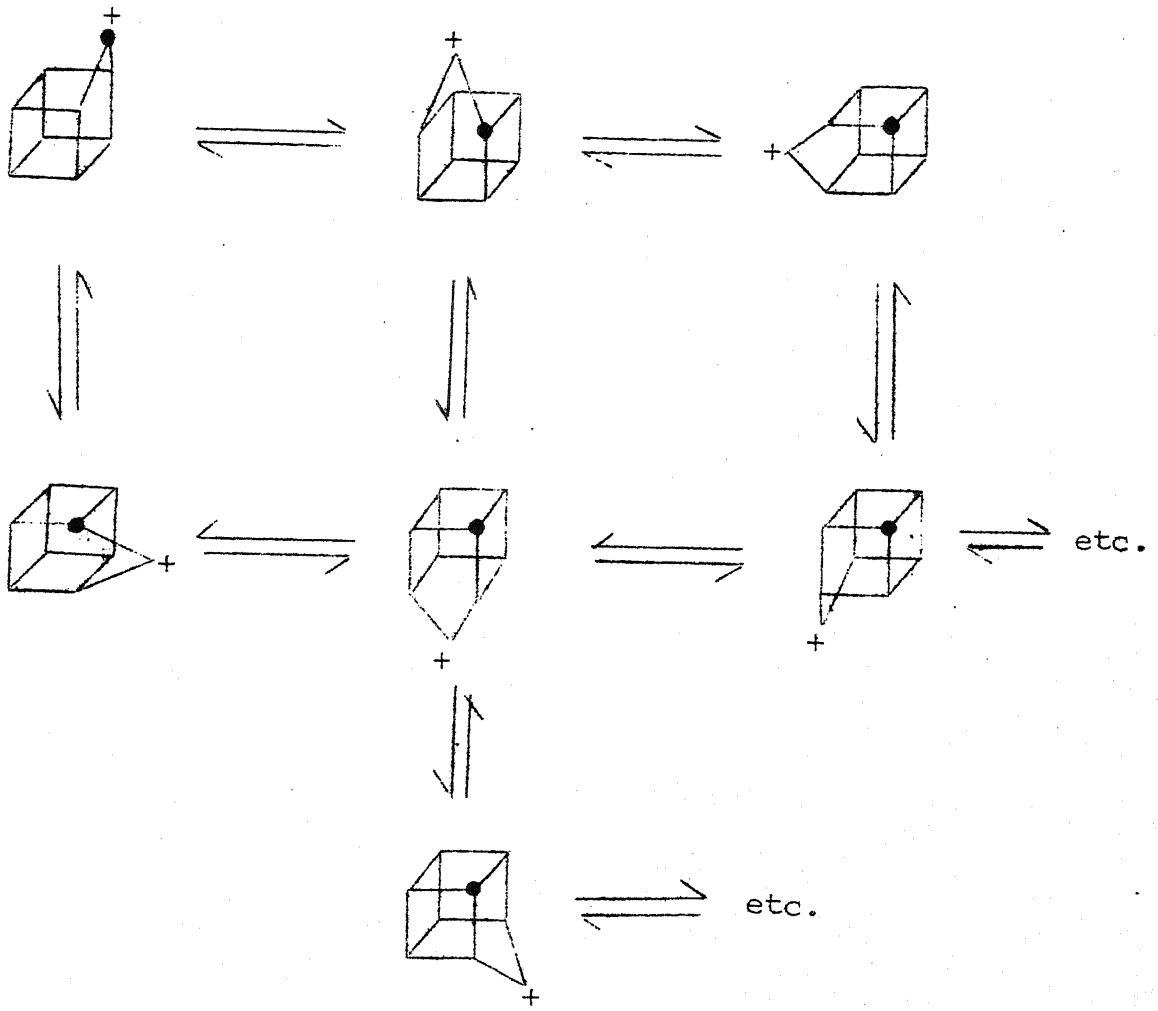
25

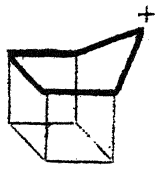
SOLVOLYTIC REACTIONS

The homocubyl systems(2, 4-8) are so constructed that creation of an electron deficient site on one of the homo-bridges can unleash a series of multiple 1,2-alkyl shifts. Furthermore, the geometry of these molecules is such that solvolysis rates of appropriate derivatives can be significantly enhanced through σ participation. This is fully borne out by the significantly high rates observed for the solvolysis of homo- and bishomocubyl tosylates[38] and mesylates[39] than that expected on the basis of ir carbonyl frequency for unassisted solvolysis (Schleyer-Foote correlation).[40,41]

Among the cubyl systems, the homocubyl cation (13) is the most interesting as it belongs to a series of homologous ions based on regular polyhedra (other possible examples are homotetrahedryl cation, $C_5H_5^+$ & homododecahedryl cation, $C_{21}H_{21}^+$) which are capable of achieving complete degeneracy by employing only 1,2- carbon shifts.[42,43] Thus, 13 represents a potentially degenerate $C_9H_9^+$ cation[42,43] in which all carbon-hydrogen units can exchange positions and become equivalent (Scheme III.2). Two distinct pathways are available to homocubyl cation (13) for achieving degeneracy. One is a non-stereospecific process leading to complete degeneracy (Scheme III.2) and the other a stereospecific process in which the bond trans to the leaving group migrates leading to five fold degeneracy.

Scheme III.2





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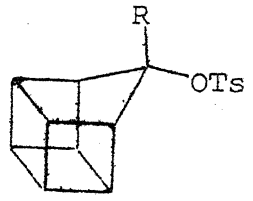
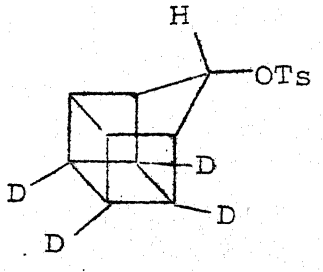


14, R=H
15, R=D

Research groups at Princeton and Smith-Kline have jointly investigated[44] the formolysis of parent 14 and 9-deutero derivative 15 and concluded on the basis of deuterium scrambling results that the ion is totally degenerate. However, doubts[45] have been expressed regarding the validity of these results. Pettit[46] on the other hand, employing the base-deuterated homocubyl tosylates (16) & (17) has shown that their solvolytic rearrangements are highly stereospecific and only the bond trans to the leaving group migrates. Thus, only the five membered ring (heavy lined in 13) goes on a merry-go-round on the four bonds supported by a cyclobutane base.



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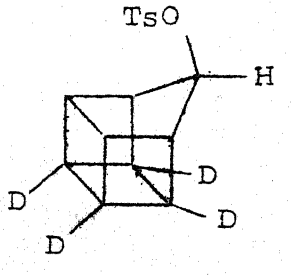
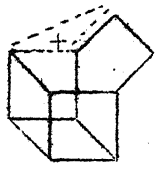


17

Solvolytic studies have also been carried out on bishomocubyl systems 4, 6 & 7. Like homocubyl cation (13), the bishomocubyl cations also undergo 1,2-alkyl migrations but in these cases the second methano bridge serves as a means of detecting the structural change. The rearrangement products obtained[38,39] from the acetolysis of mesylates 18 & 19 and tosylates 20 & 21 are shown in Scheme III.3. The rate of solvolysis of all bishomocubyl systems is accelerated by a factor of 10^2-10^5 compared to the value calculated for the nonassisted solvolysis according to Schleyer-Foote correlations. The enhanced rates have been attributed to the anchimeric assistance by the neighbouring σ bond and ions 22, 23 & 24 have been postulated[38,39,47] as intermediates in the case of solvolysis of 18, 20 & 21, respectively.



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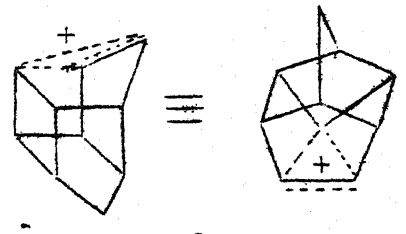

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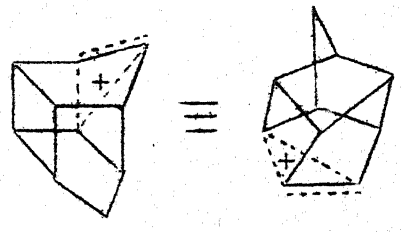
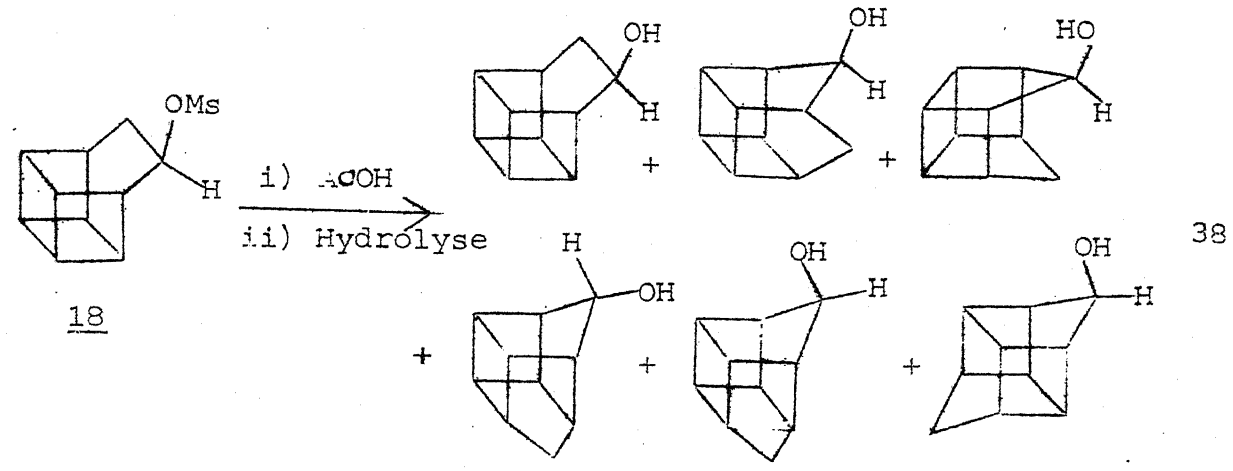


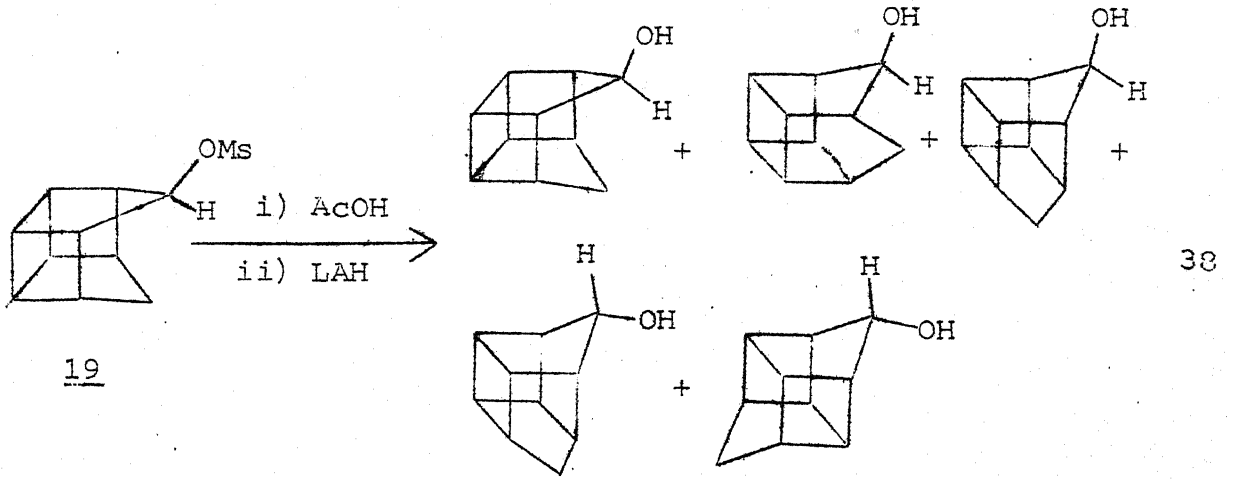
24

Scheme III.3

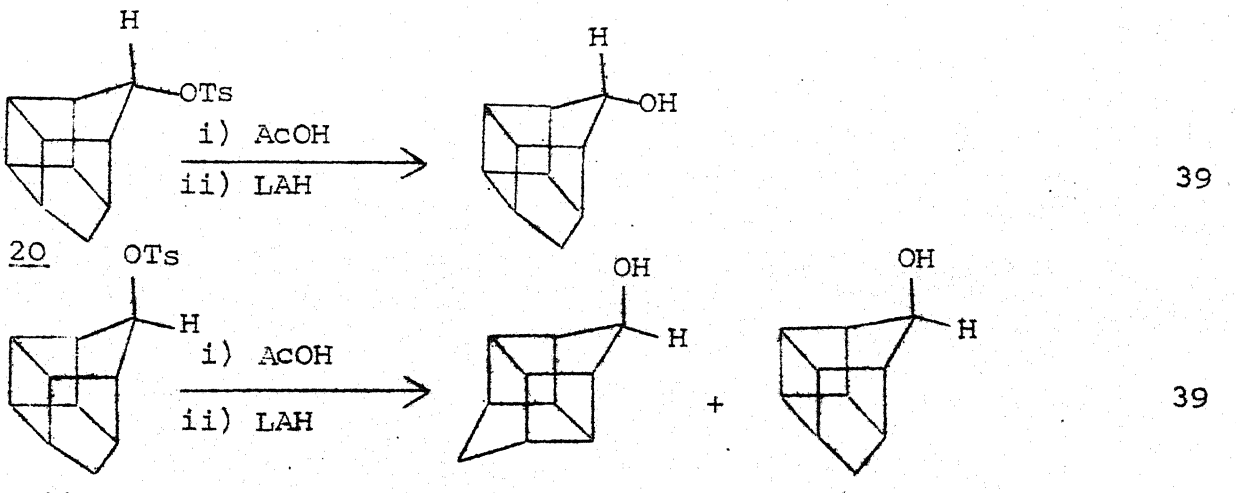
Ref.



18 38



19 38

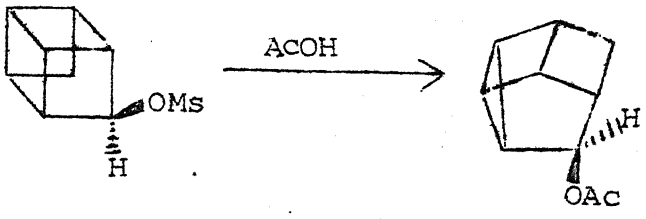


20 39

21 39

Lastly, Dauben and Reitman[19] have recently synthesised exo-secocubyl mesylate (25) and studied its solvolysis. The mesylate 25 on acetolysis furnished the acetate 26 as the major product in near quantitative yield (Scheme III.4):

Scheme III.4



25 26

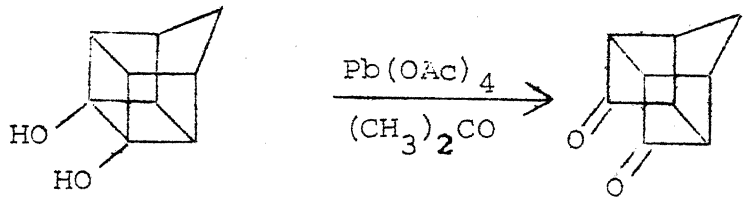
MISCELLANEOUS REACTIONS

Several interesting chemical transformations and rearrangements of cubyl systems 1- 8 and their derivatives have been discovered in past few years. Many of these are mechanistically fascinating and provide easy access to many novel carbocycles. These transformations are best appreciated and enjoyed as depicted schematically in Scheme III.5.

Among the various cubyl systems, 1,3-bishomocubane (6) and 1,3-bishomocubanone (27) in particular are most readily[64,65] obtainable. The pentacyclic ketone (27) is conveniently prepared[64] in three steps from commercial dicyclopentadiene (28, Scheme III.6). However, despite the ready availability of 27, its chemistry has only received limited attention (examples cited in Scheme III.5). A programme was therefore initiated[62,63]

Scheme III.5

Ref.



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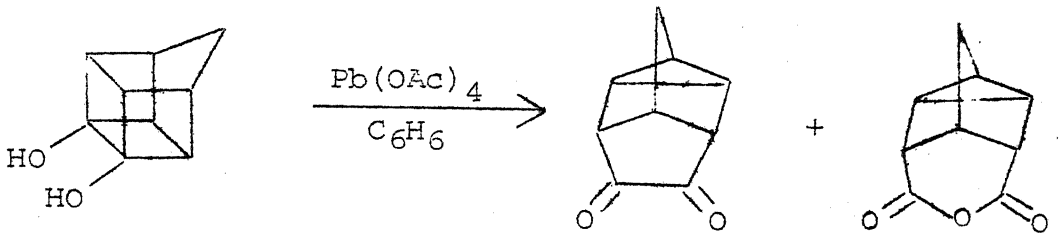

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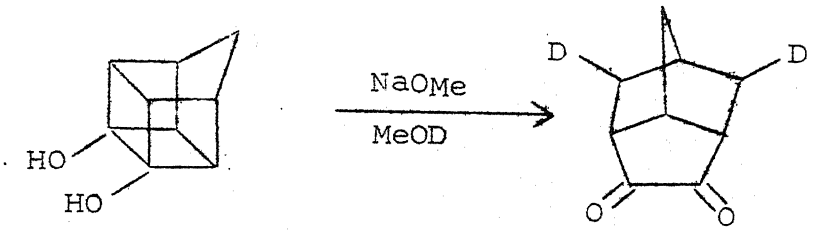

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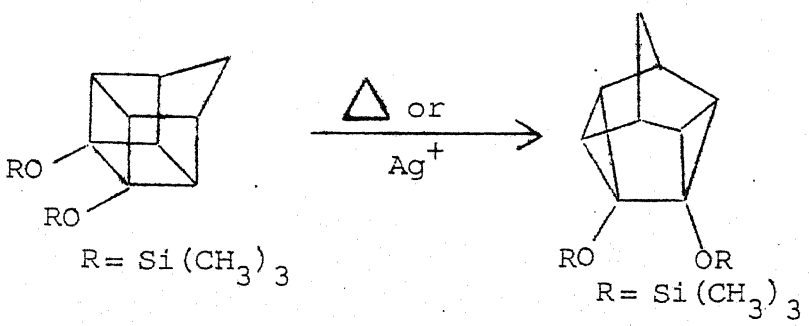

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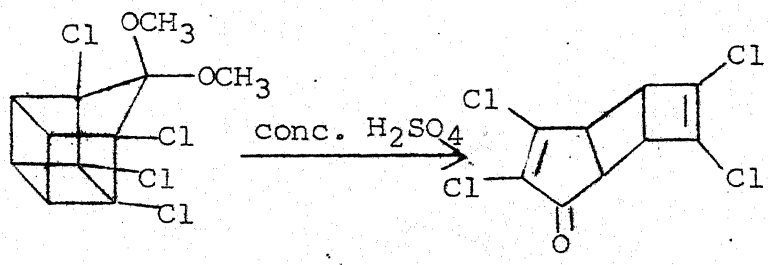

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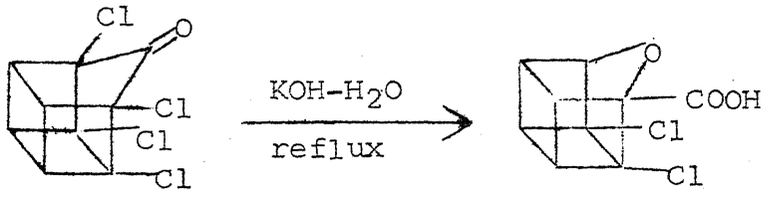

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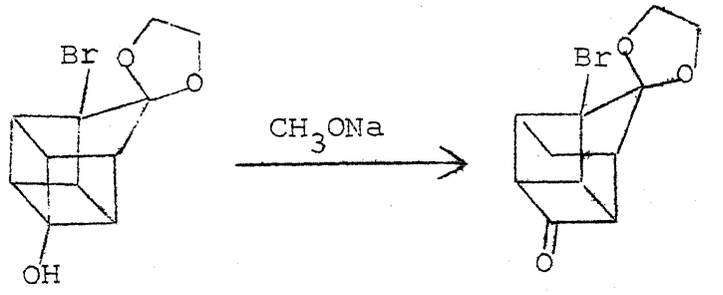

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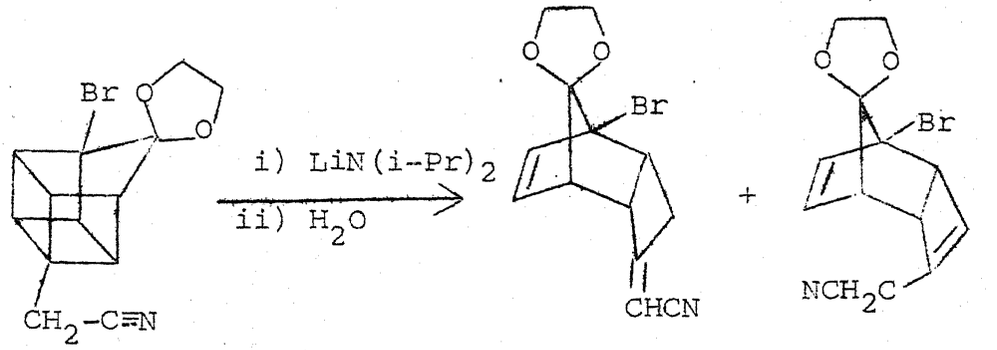

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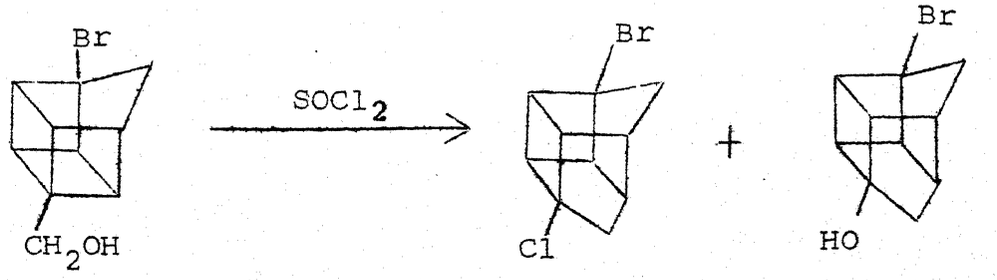

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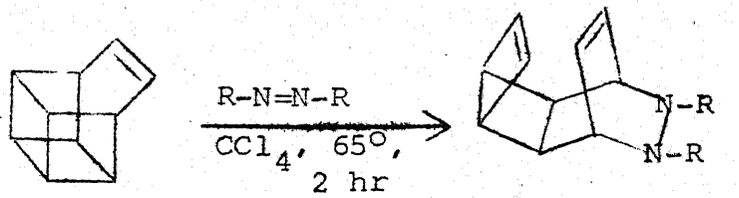

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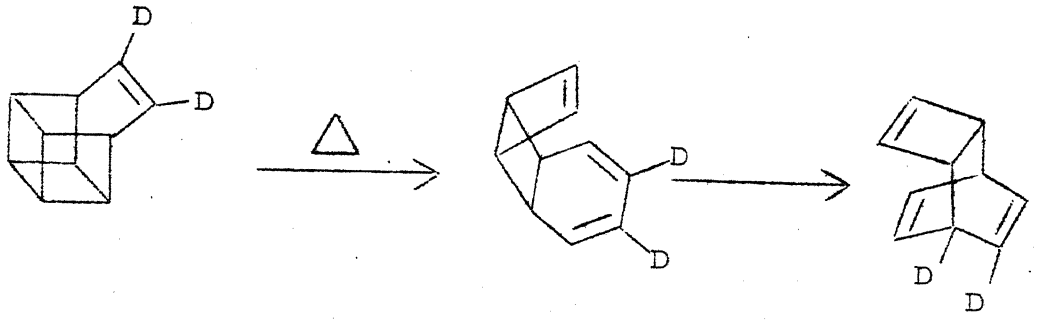

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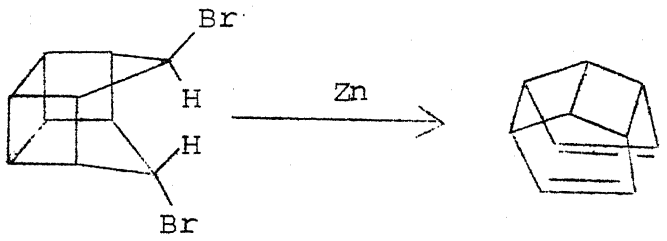

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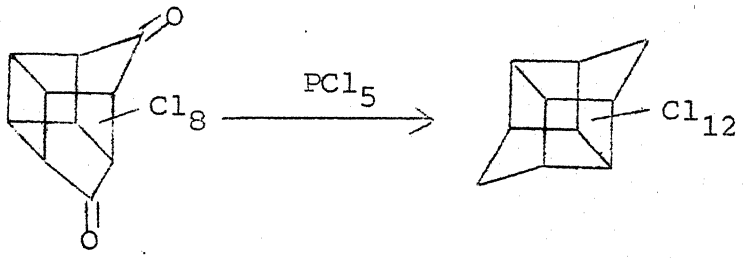

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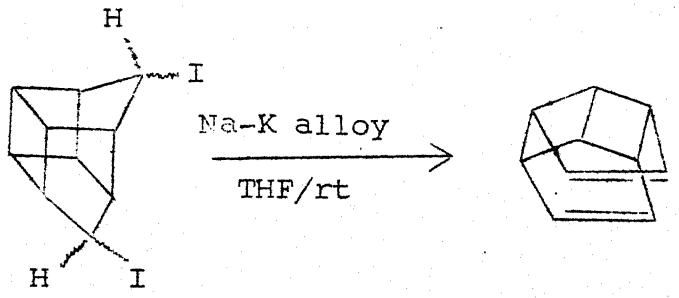

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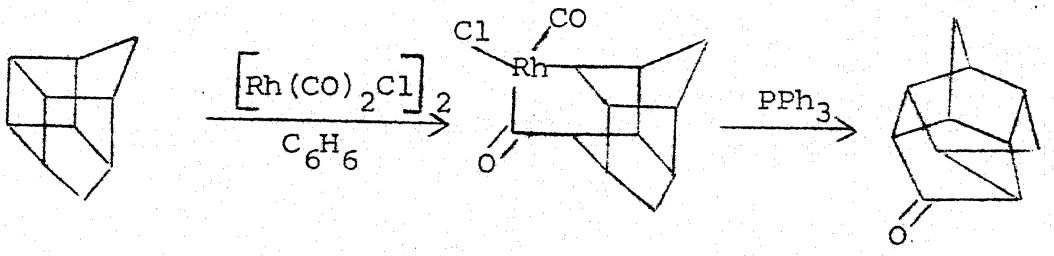

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Scheme III.5 (contd.)

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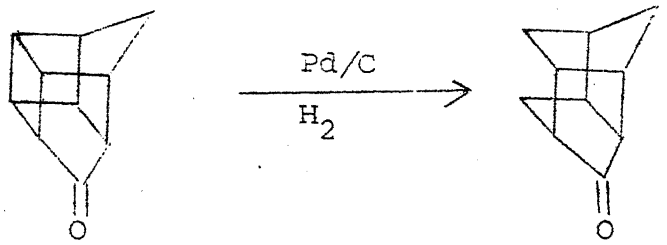

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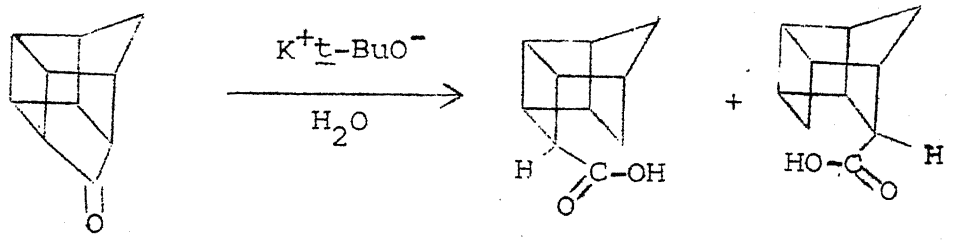

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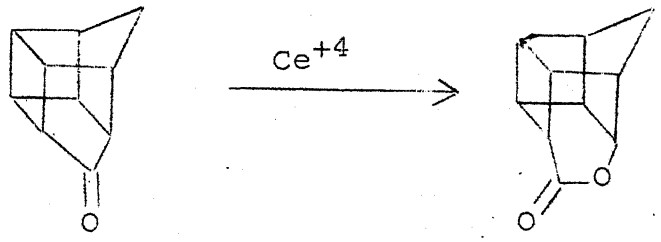

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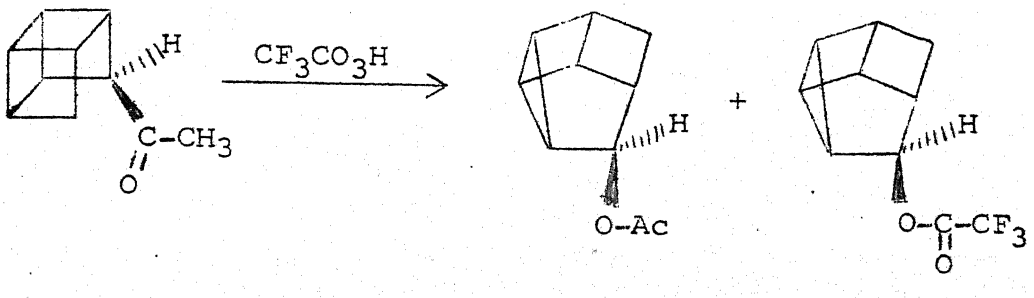
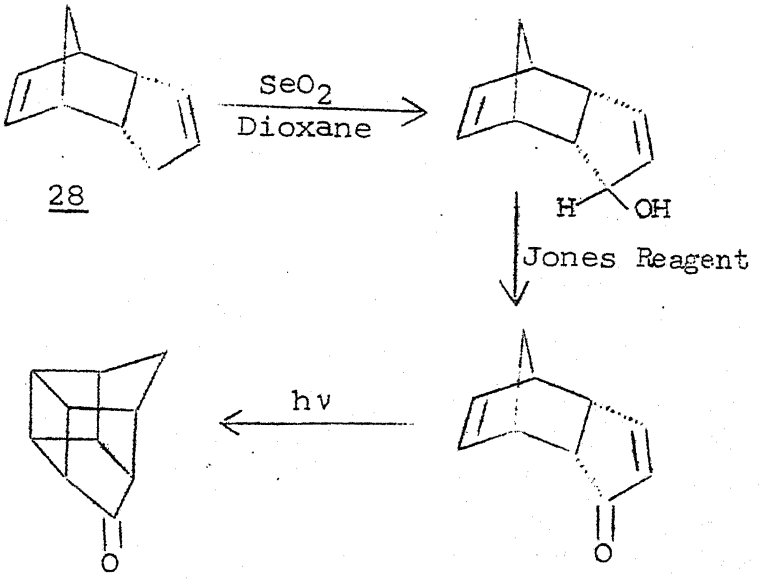


19

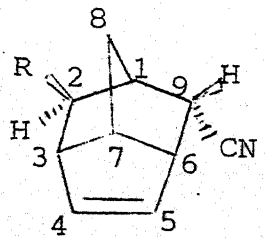
in our laboratory to study various transformations of 27 with particular emphasis on rearrangements and fragmentation reactions. In this chapter of the thesis, a novel,unanticipated transformation of 1,3-bishomocubanone (27) to 2,9-disubstituted brend-4-ene derivative 29, under Schmidt reaction conditions is described. Some interesting reactions of brendene derivative 29 are also discussed:

Scheme III.6



28

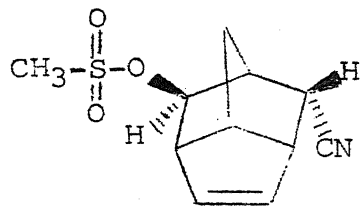
27



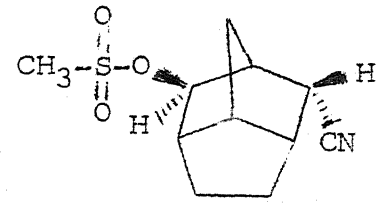
29

III.3 RESULTS AND DISCUSSION

Reaction of 1,3-bishomocubanone (27) with hydrogen azide in methanesulphonic acid furnished a crystalline mesylate 30, mp 88° in 45% yield. The structure of 30 has been deduced from spectral and chemical evidence discussed below:



30



31

The mesylate 30 analysed correctly for $C_{11}H_{13}NO_3S$ and showed in its mass spectrum the highest mass peak at M^+ 239, which is consistent with its molecular formula. The ir spectrum (Fig. III.1) was quite informative and revealed the nature of the functional groups. Thus, the presence of a cyano group (2245 cm^{-1}) and a sulphonate ester group (1340 & 1175 cm^{-1}) was clearly indicated by the diagnostic[66] ir bands. The pmr spectrum (Fig. III.2) displayed a 2H olefinic proton multiplet centred at δ6.2. The presence of a sulphonate ester functionality was confirmed by the presence of sharp singlets at δ3.1 (3H) and δ4.6 (1H) due to the methyl group and proton adjacent to the methanesulphonoxy group, respectively. The rest of the pmr spectrum consisted of a quartet centred at δ1.9 (J_{gem} = 11 Hz) due to non-equivalent methylene protons and a cluster of peaks between 2.7- 3.4 due to the rest of the ring protons.

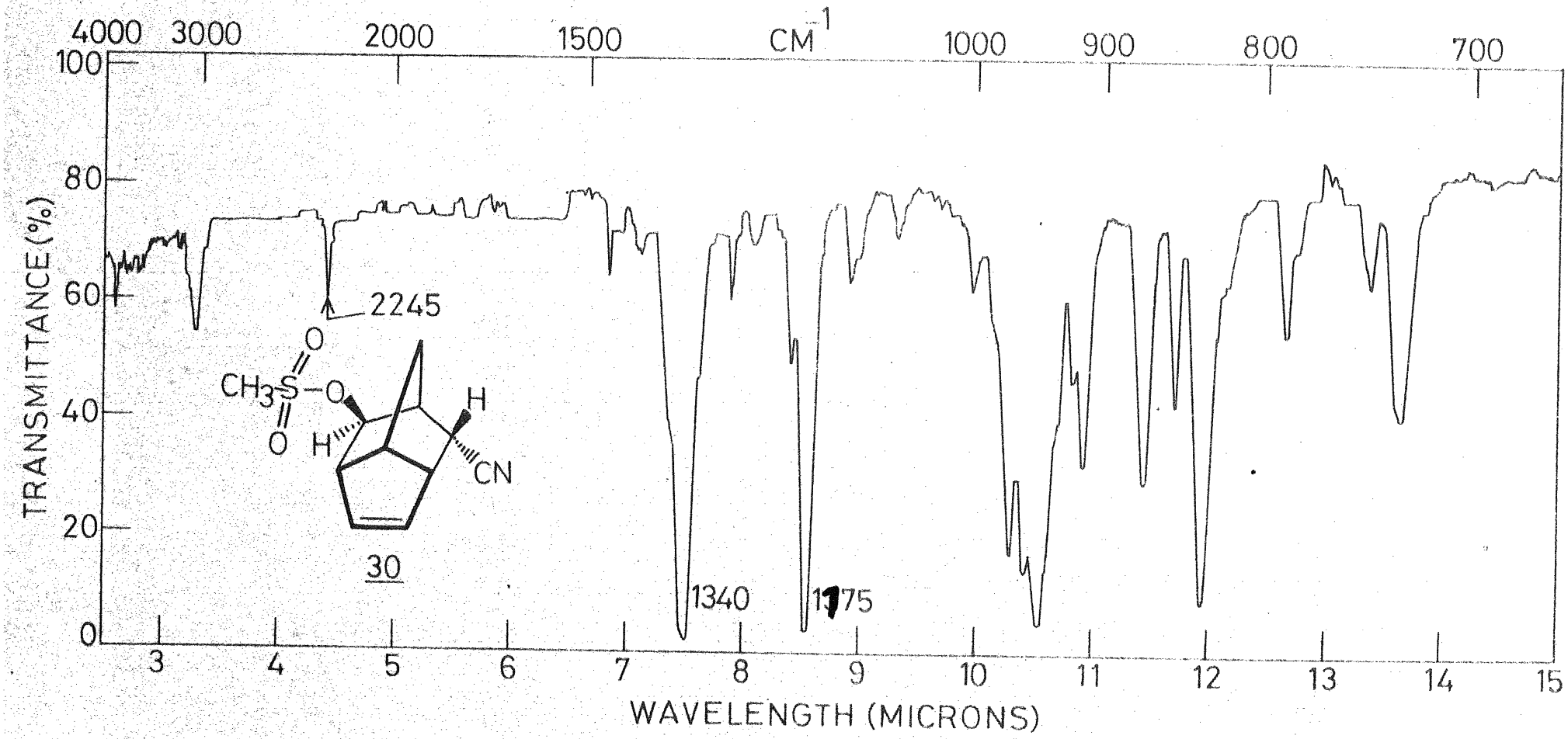
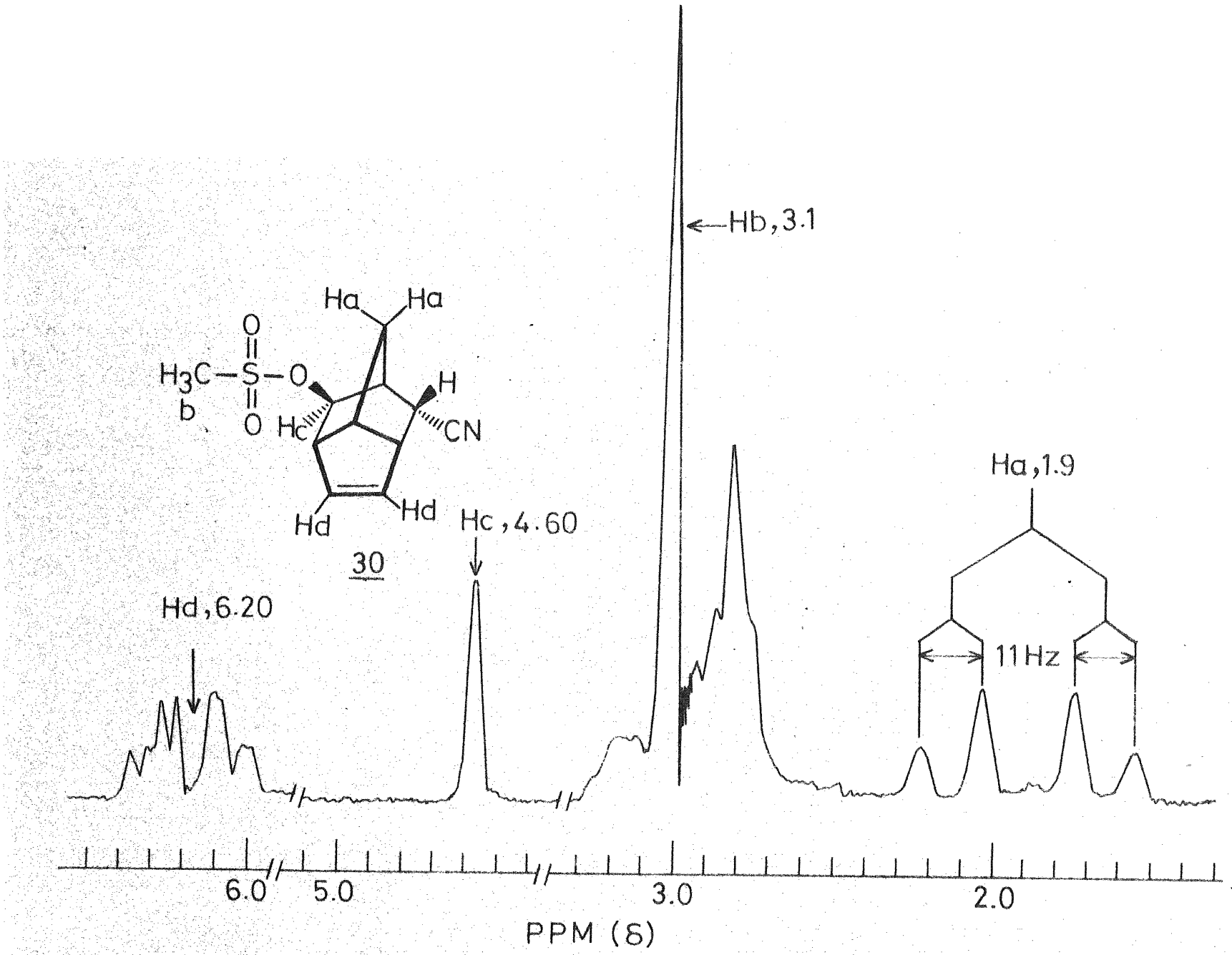


Fig. III.1 IR spectrum (KBr) of 30



30

Fig. III.2 PMR spectrum of (60 MHz) of 30

Catalytic hydrogenation of 30 over Pd-C(10%) catalyst resulted in uptake of one mole of hydrogen and furnished a dihydro derivative 31, mp 79°. The dihydroderivative analysed for $C_{11}H_{15}NO_3S$ (M^+ 241) and being saturated must be a tricyclic compound. The pmr spectrum (Fig. III.3) of the dihydromesylate (31) was transparent in the olefinic proton region but the signals due to the methyl group (δ3.03, 3H, s) and the proton (δ4.4, 1H, s) attached to the methanesulphonoxy group were conspicuously present. The quartet at δ1.84 (J_{gem} = 11 Hz) due to the nonequivalent methylene group was superimposed by a broad singlet (δ1.9, 4H) resulting from the saturation of the disubstituted olefinic linkage of 30 to a pair of $-CH_2-$ groups. The ir spectrum (Fig. III.4) showed expected bands at 1330, 1170 (sulphonate ester) and 2240 cm^{-1} (cyano) but was devoid of absorptions due to olefinic linkage.

Besides 30, the foregoing spectral data in conjunction with mechanistic considerations is suggestive of several tricyclic structures (32, 33, 34, 35 & 36), derivable from intermediate 37 through two bond dislocations and capture by the mesylate anion as shown in Scheme III.7. Among these only tricyclo[4.2.1.$0^{3,7}$]non-4-ene (brendyl skeleton,[67] 30), tricyclo[4.3.0.$0^{3,8}$]non-4-ene (twist brendyl skeleton,[68] 34) and endo-tricyclo[4.2.1.$0^{2,5}$]non-7-ene[69] (33) type structures merit serious consideration for the product derived from 27. The rest of the structures 32, 35 & 36 can be discounted on the basis of the pmr multiplicity[70] of olefinic proton signal

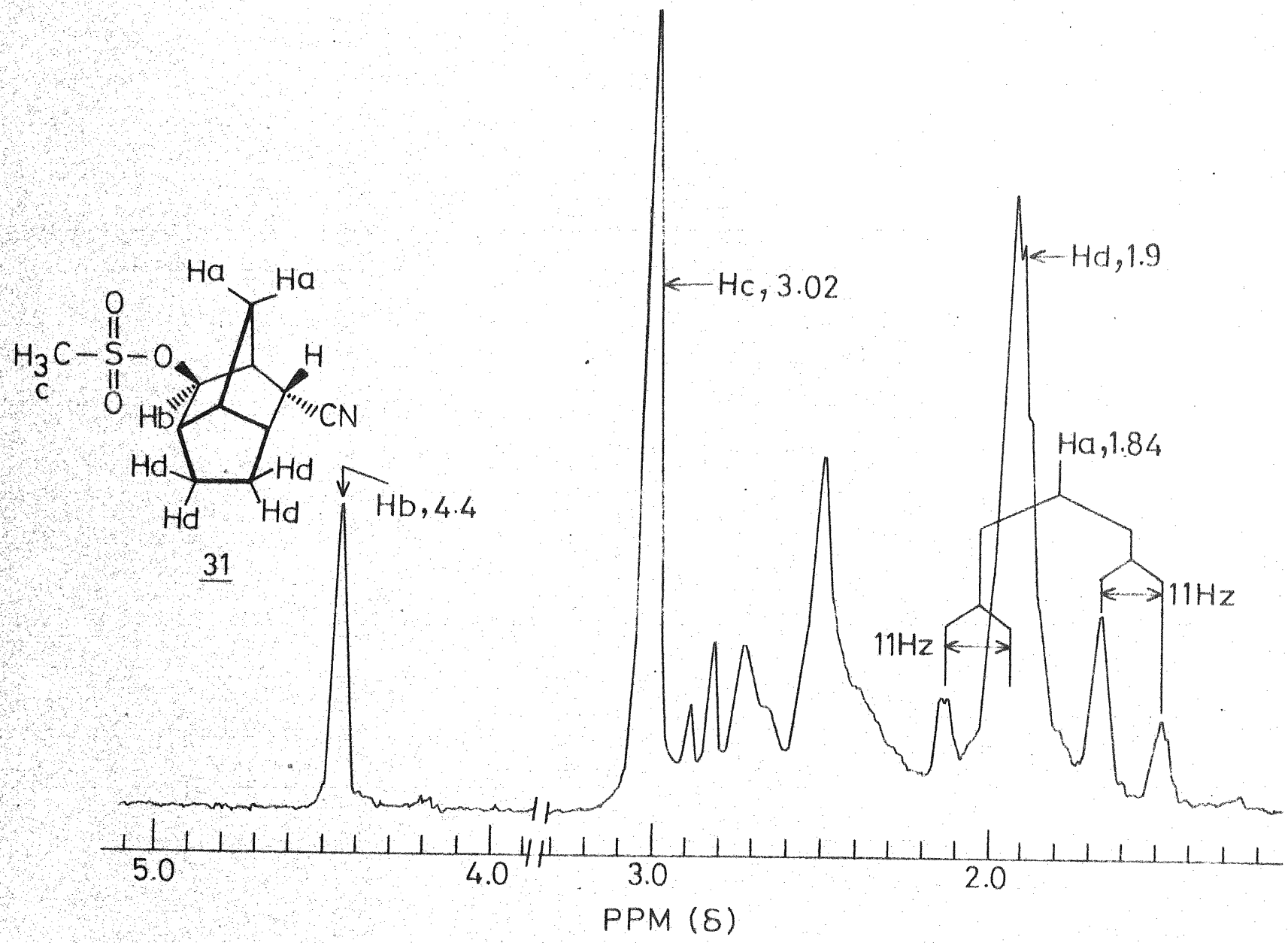


Fig. III.3 PMR spectrum (60MHz) of 31

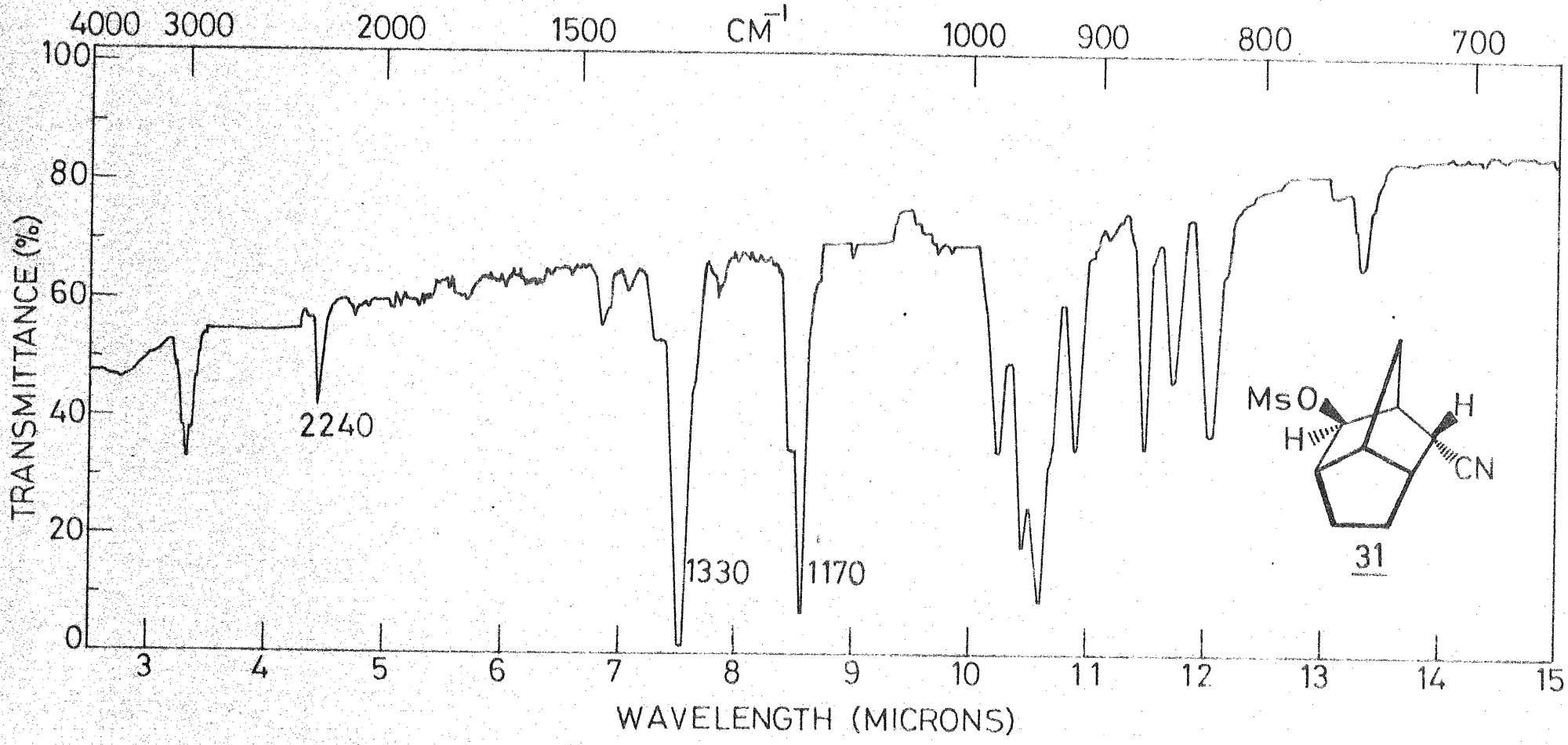
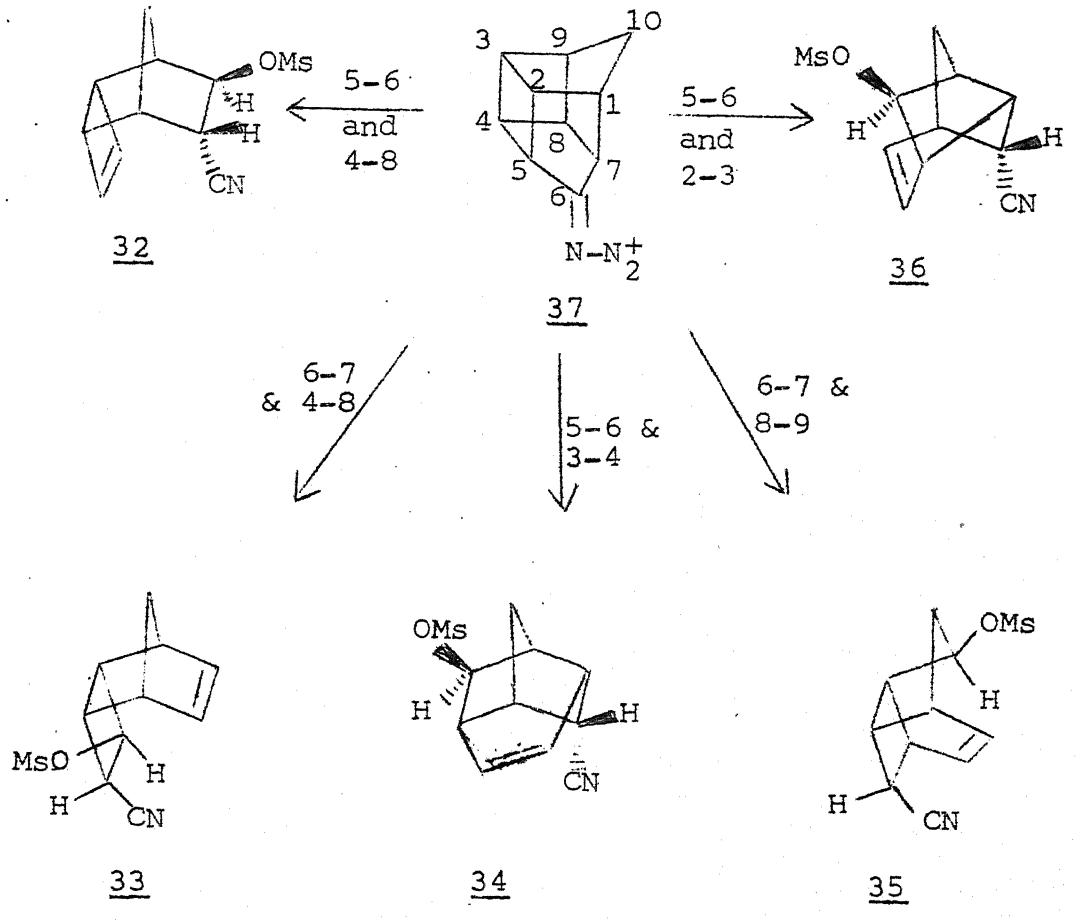


Fig. III.4 IR spectrum (KBr) of 31

and the singlet nature of the proton attached to the methanesulphonoxy group. This surmise is further strengthened by the series of reactions summarised in Scheme III.8.

Scheme III.7

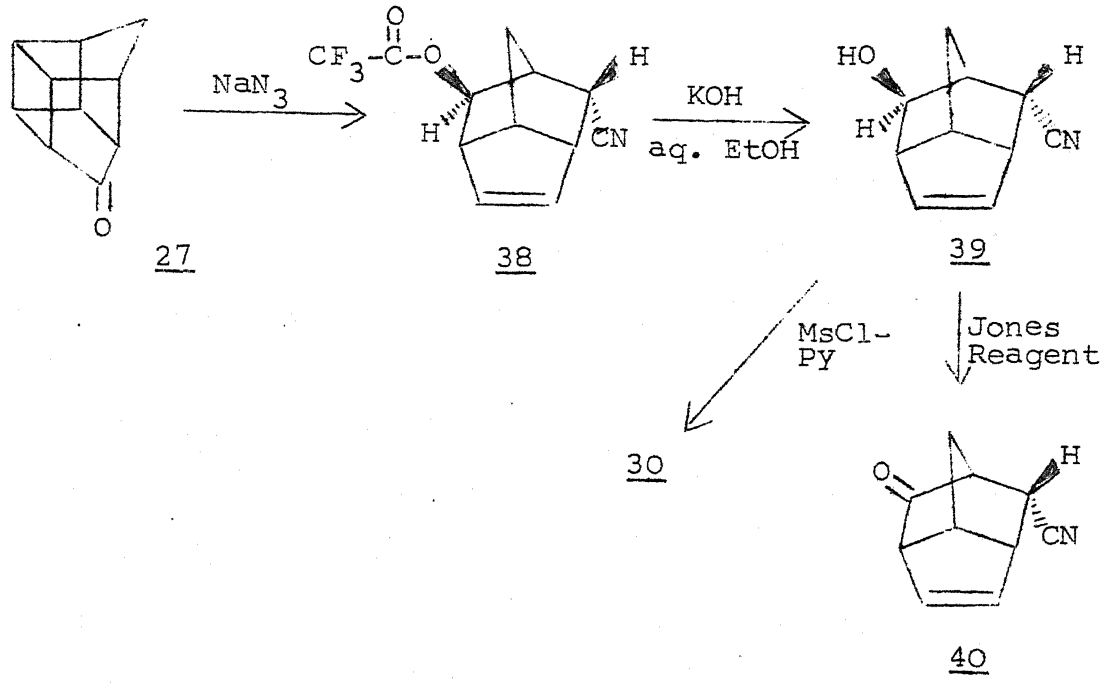


32 37 36

33 34 35

Reaction of 27 with hydrogen azide in trifluoroacetic acid medium furnished the trifluoroacetate(38), though the reaction was not as clean as in the methanesulphonic acid medium. Mild base hydrolysis of 38 yielded the tricyclic

Scheme III.8



27 38 39 30 40

alcohol 39, mp 44-6° (3:5 dinitrobenzoate, mp 192°).* The ir spectrum of 39 exhibited bands at 3475, 1045 (hydroxyl) and 2245 cm^{-1} (cyano group). The pmr spectrum displayed a 2H olefinic proton multiplet centred at δ6.11 together with a 1H singlet at δ3.75 due to the proton attached to the hydroxyl group. The alcohol 39 could be easily transformed into mesylate 30 with mesyl chloride in pyridine, thus establishing the similar nature of product obtained in methanesulphonic acid and

*The crystal structure of this 3:5-dinitrobenzoate is being investigated by Dr. K. Venkatesan, Indian Institute of Science, Bangalore using X-ray diffraction technique. His preliminary findings are in agreement with the assigned brendyl structure. We thank Dr. Venkatesan for this information.

trifluoroacetic acid medium. Lastly, oxidation of 39 with Jones reagent gave tricyclic ketone (40) exhibiting cyclopentanone absorption (1750 cm^{-1}) in the ir spectrum.

A distinction between structures 30, 33 & 34 for the mesylate obtained from 27 could be achieved through a facile base catalysed elimination reaction. Brief exposure of 30 to potassium ter-butoxide in DMSO resulted in the elimination of the mesyl group and a liquid cyano compound, $C_{10}H_9N$, was obtained. The pmr spectrum (Fig. III.5) of the elimination product still exhibited only two olefinic protons as a narrow triplet at δ6.18 (J = 1.5 Hz), indicating equivalence of chemical shift and coupling constants. The nature of the other resonances in the pmr spectrum were further suggestive of a skeletal rearrangement during the elimination step. Specifically, the presence of only two olefinic protons clearly indicated the formation of a new ring during the elimination step. A consideration of structures 30, 33 & 34 for the mesylate reveals that only the brendene derivative 30 is suitably poised for a 1,3-elimination to tetracyclo[4.3.0.$0^{2,4}$.$0^{3,7}$]non-8-ene[71] (deltacyclene[71]) derivative 41 (Scheme III.9). The alternate tricyclic structure 33 would have led to elimination product 42 with three olefinic protons. Similarly, the twist brendene 34 is better disposed for a base catalysed fragmentation to dihydro indene derivative 43.

Further support for the deltacyclene structure 41 was derived from the ir spectrum (Fig. III.6) which displayed bands

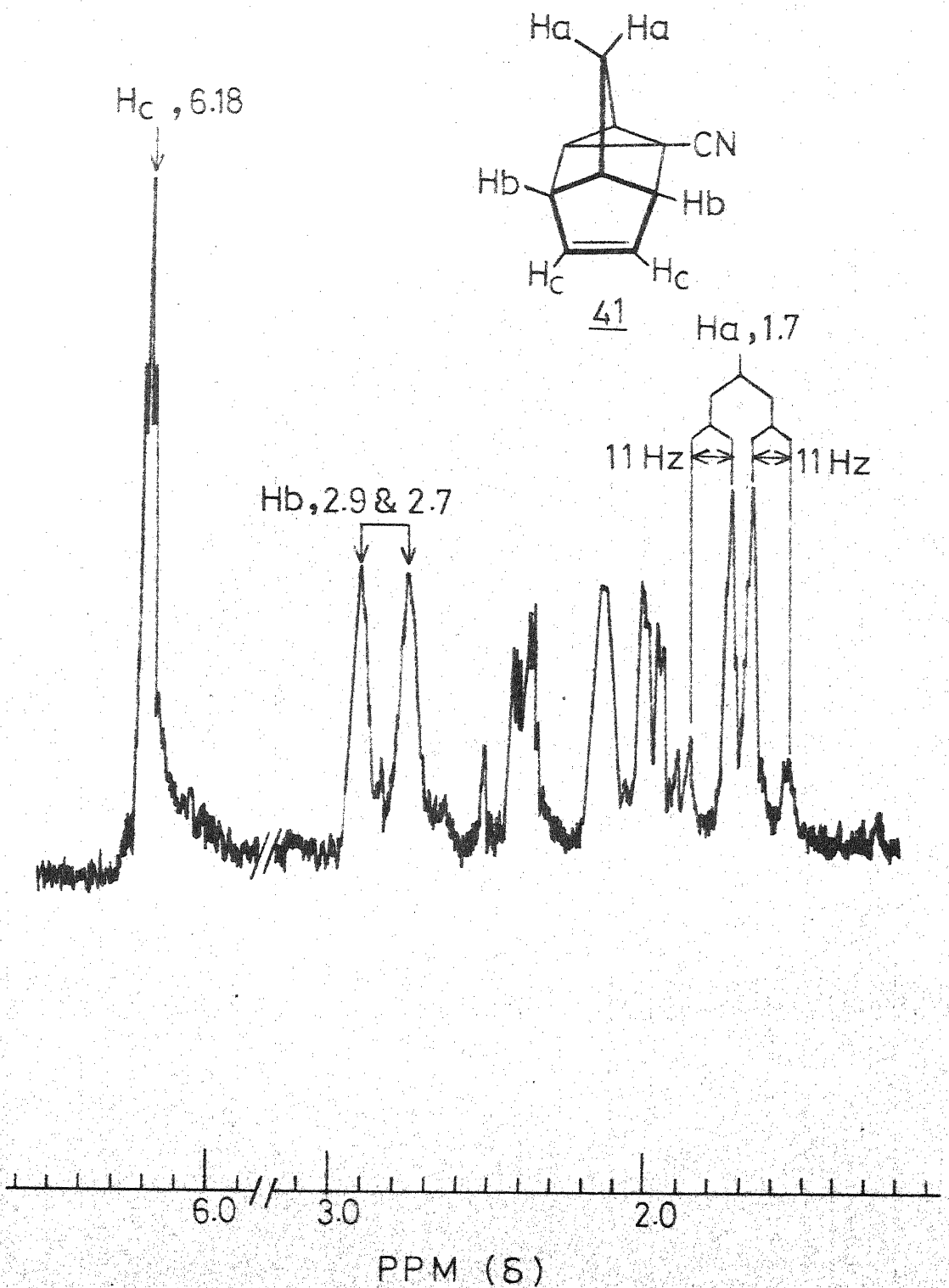


Fig. III.5 PMR spectrum (100 MHz) of 41

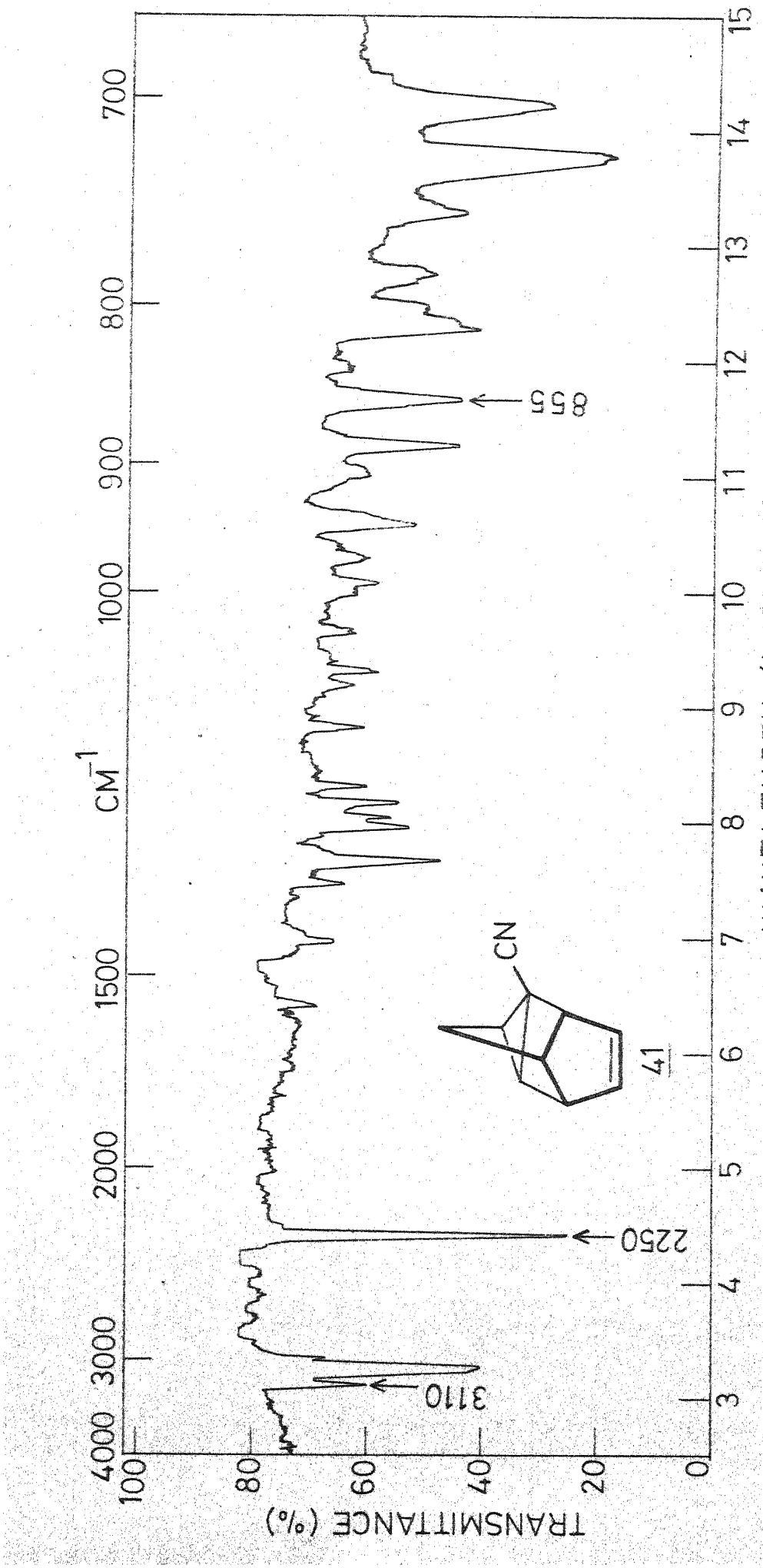
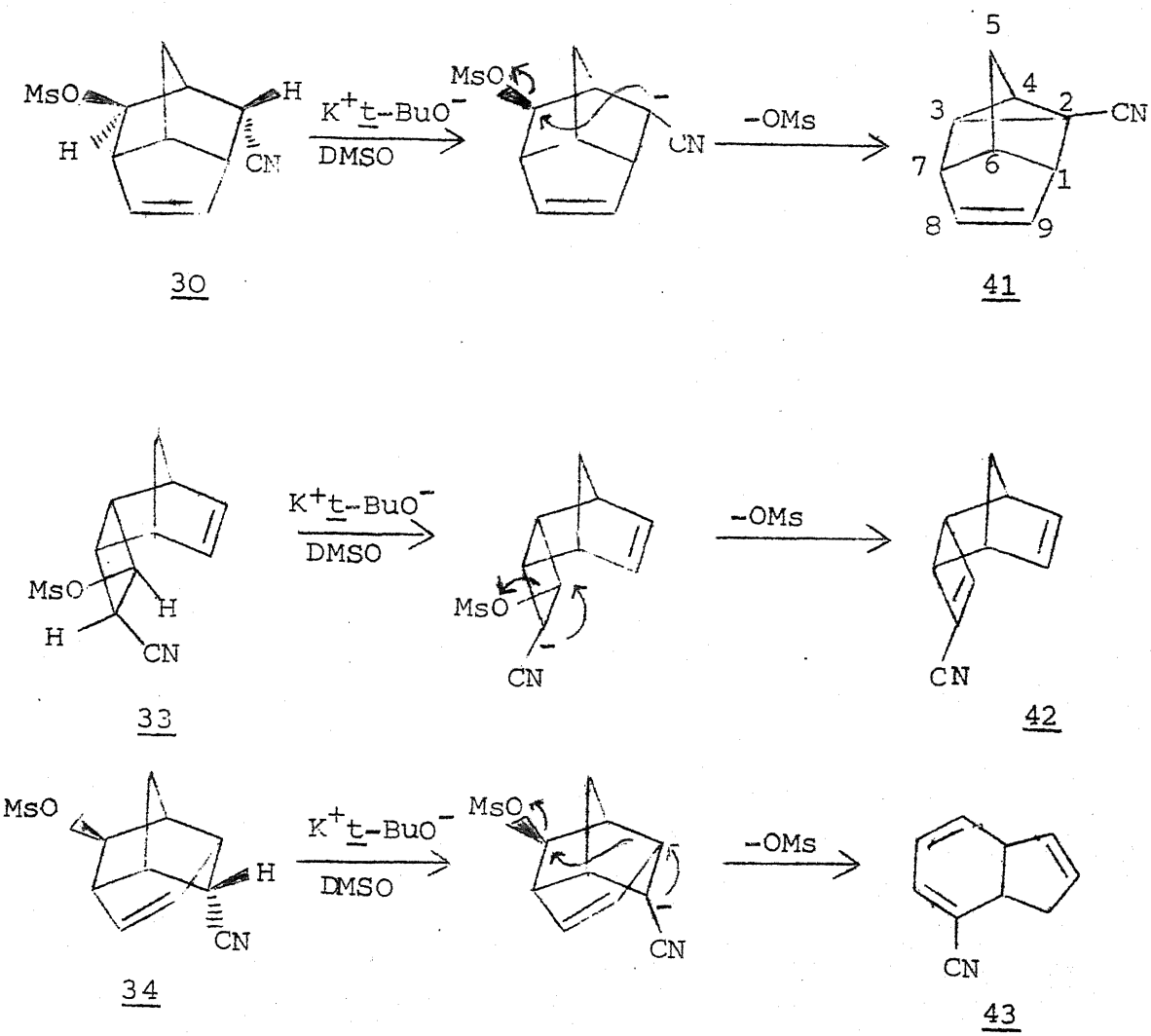


Fig. III.6 IR spectrum (neat) of 41

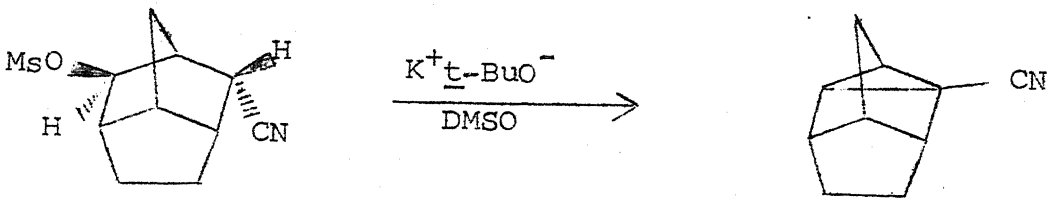
Scheme III.9



at 3110 (cyclopropane CH) and 855 cm^{-1} (tricyclene type nucleus) along with strong band at 2250 cm^{-1} (cyano group). The various signals in the pmr spectrum of 41 were quite distinctive and assignments could be provisionally made through comparison of signals with various deltacyclenes reported in literature.[72,73]

In confirmity with 1,3-elimination observed for 30, the dihydro mesylate 31 also underwent facile elimination to deltacyclane 44 (Scheme III.10). The absence of any pmr or ir

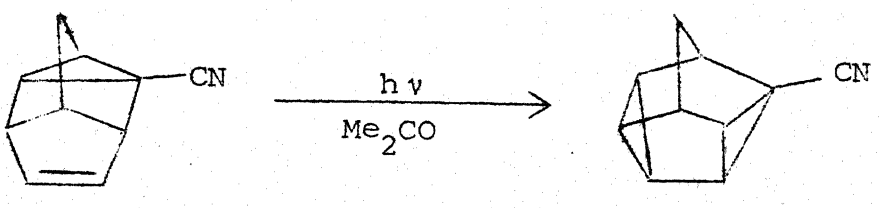
Scheme III.10



31 44

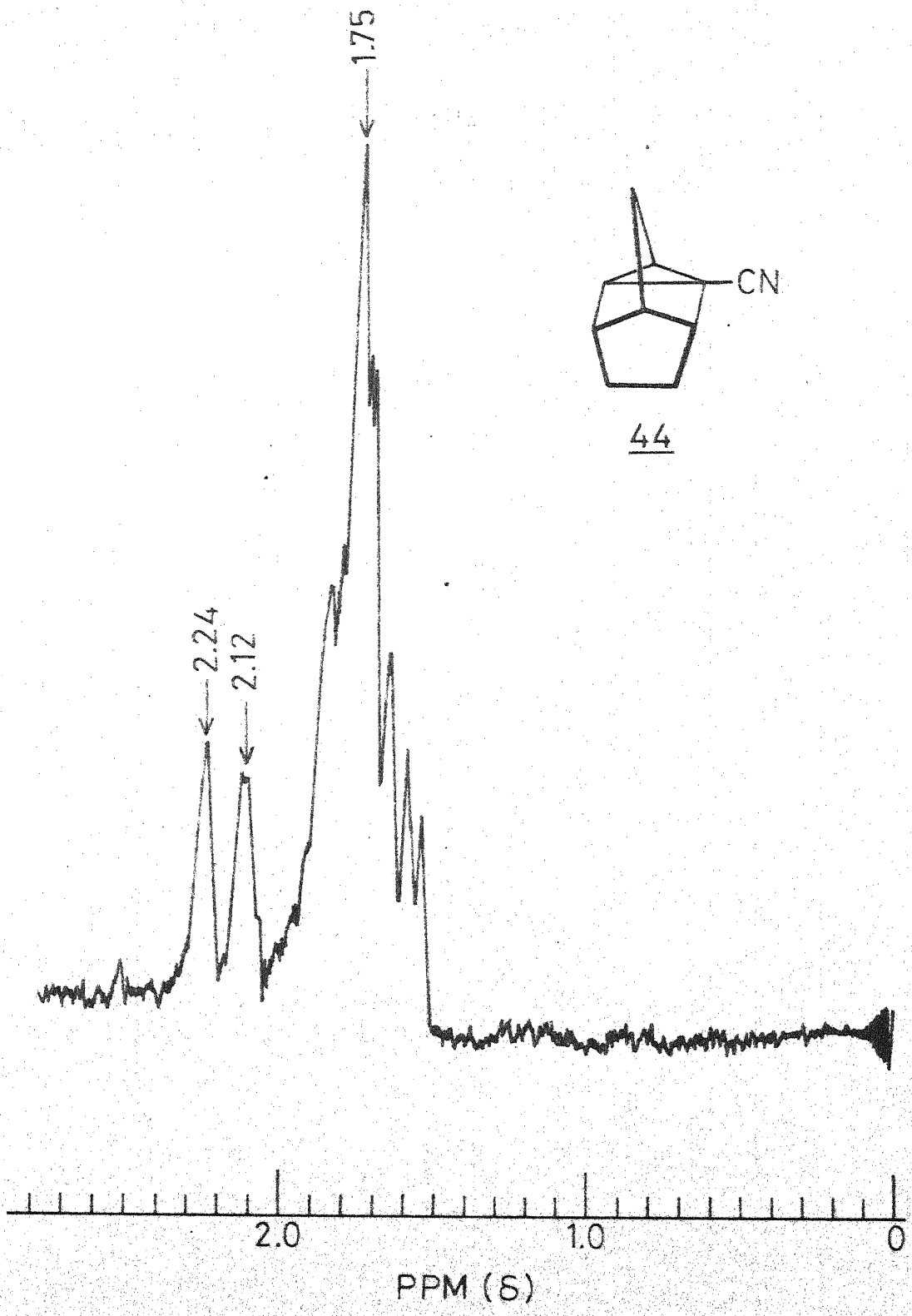
evidence for unsaturation suggested that the new structure was a tetracyclic system. The pmr spectrum (Fig. III.7) of 44 showed only three resonances at δ2.24, 2.12 & 1.72 in a ratio of 1:1:9. The ir spectrum (Fig. III.8) with characteristic absorptions (3075, 855 cm^{-1}) confirmed the presence of a cyclopropane ring. The final confirmation of the structure of deltacyclene derivative 41 and its precursor mesylate 30 was achieved through its acetone sensitised photochemical valence isomerisation to the pentacyclic norsnoutane derivative 45 in nearly 76% yield (Scheme III.11). The pmr spectrum of 45 was

Scheme III.11



41 45

transparent in the olefinic proton region and only showed peaks in the δ1.24-2.24 region due to ring methine protons and deshielded cyclopropane hydrogens which resonate in this region



44

Fig. III. 7 PMR spectrum (100 MHz) of 44

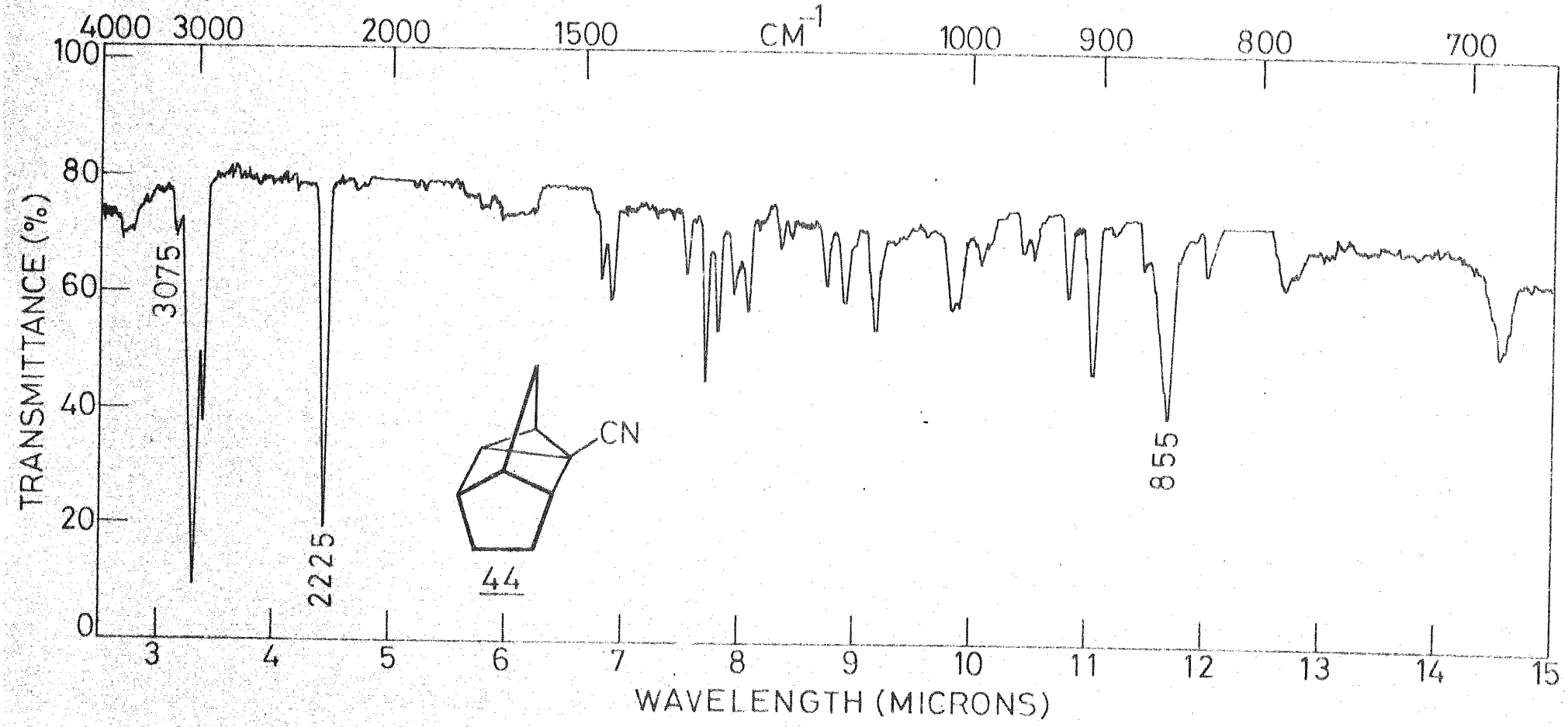


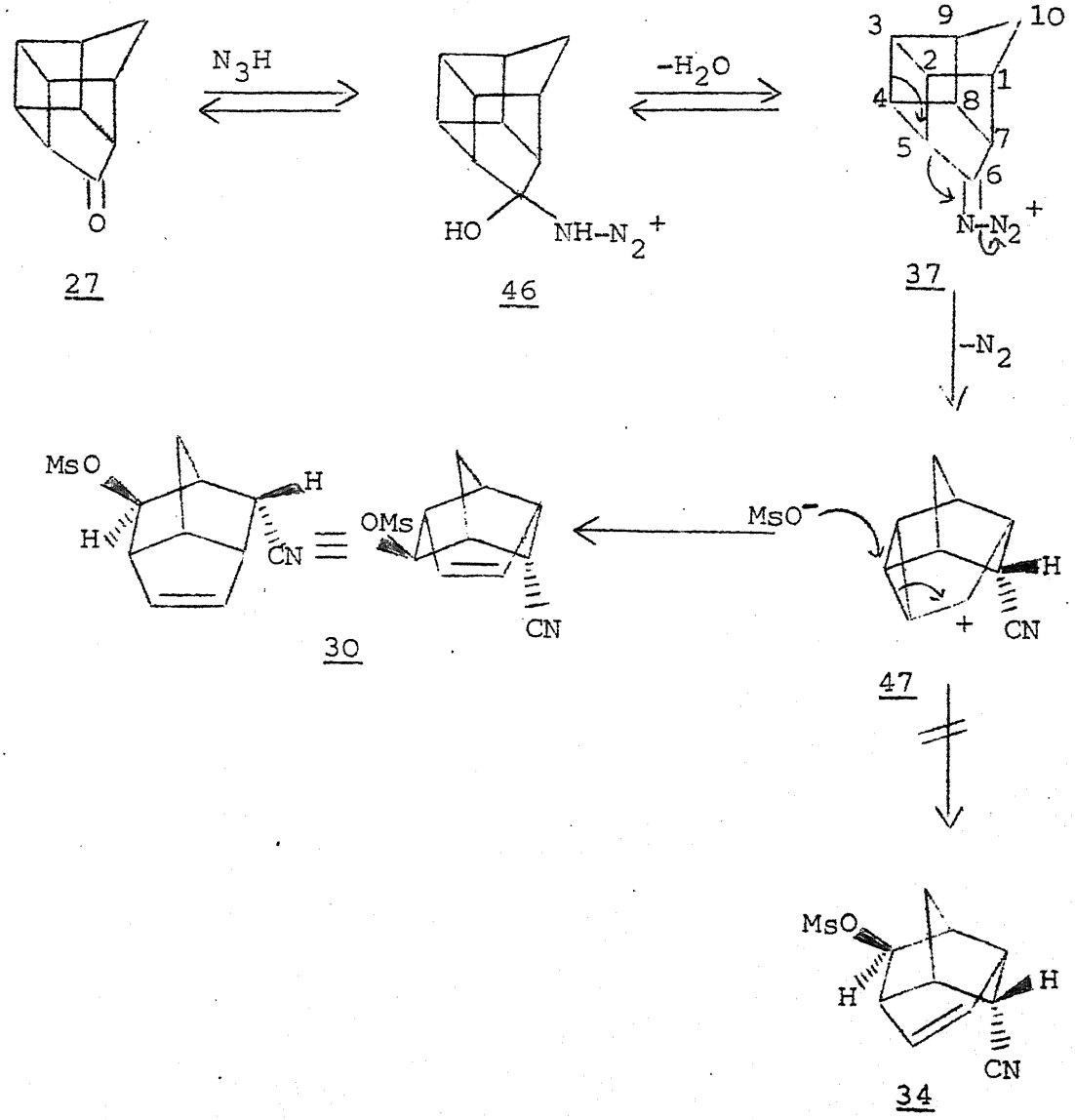
Fig. III.8 IR spectrum (neat) of 44

in several norsnoutane derivatives. The photochemically induced $\sigma^2s + \pi^2s$ cycloaddition of deltacyclenes to norsnoutanes is well precedented and numerous examples[74-79] are documented in the literature.

A reasonable mechanism for the genesis of exo-2-methanesulphonoxy-endo-9-cyanobrend-4-ene (30) from 1,3-bishomocubanone (27) during Schmidt reaction conditions (NaN_3-$CH_3.SO_2OH$) is depicted in Scheme III.12. The key intermediate 37 for Schmidt fission is readily formed via nucleophilic addition of azide ion (N_3^-) to the protonated carbonyl of 27 to azidohydrin (46) followed by acid catalysed dehydration. Loss of nitrogen and fragmentation of 37 with concomitant participation by C_3-C_4 bond leads to the stabilised cyclopropylcarbinyl cation (47). Mesylate ion mediated opening of the cyclopropane ring in 47 from the exo face leads to the observed brend-4-ene derivative (30). The proposed mechanism also accounts for the exo-and endo-stereochemistry of the methanesulphonoxy and cyano groups, respectively.

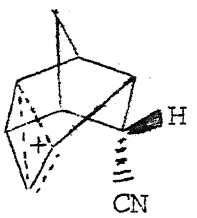
Two facets of the mechanism leading to 30 from 27 deserve special consideration. The first is the selective cleavage of the C_5-C_6 bond in preference to the C_6-C_7 bond in intermediate 37 and second is the regiospecific opening of the cyclopropane ring in carbonium ion 47 leading exclusively to 30 and not 34. It seems reasonable to propose that the cleavage of C_5-C_6 bond is assisted by the C_3-C_4 σ- bond

Scheme III.12



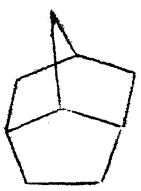
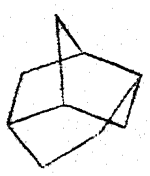
participation resulting in the formation of ion 48, stabilised through cyclobutyl – cyclopropylcarbinyl carbonium ion type resonance. Furthermore, the carbocyclic skeleton represented by 47 is relatively less strained as the bicyclo[2.2.0]-hexane moiety of 37 is transformed (two cyclobutanes → cyclopropane + cyclopentane) to a bicyclo[3.1.0]hexane system in

47. The regiospecific opening of 47 to brendyl[67] system 30 in preference to the twistbrendyl[68] system 34 reflects the greater thermodynamic stability of the former ring system. Results of recent force field calculations by Schleyer[80] and Allinger[81] attribute greater stability to brendane (49) as compared to twistbrendane (50) (Table III.1).



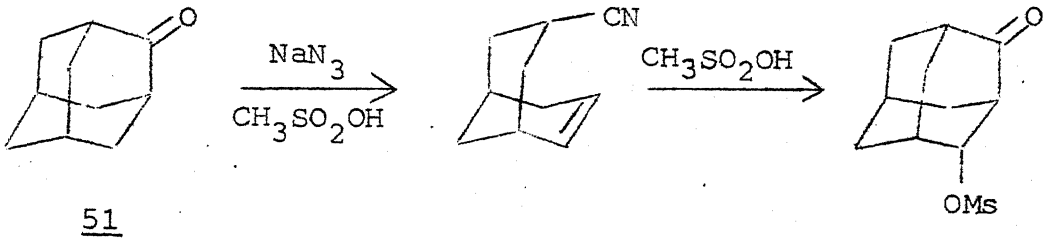
48

Table III.1. Calculated enthalpies and strain energies for brendane (49) and twistbrendane (50) (kcal/mol)

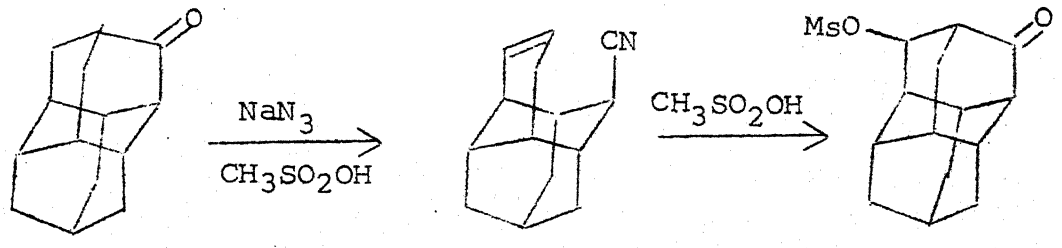
Compound	Calcd H_f° (gas, 25°)		Calcd stain energy (gas, 25°)	
	Schleyer	Allinger	Schleyer	Allinger
 Tricyclo[4.2.1.$0^{3,7}$]-nonane (49)(Brendane)	-11.72	-10.31	22.57	24.26
 Tricyclo[4.3.0.$0^{3,8}$]-nonane (50) (Twist brendane)	-0.12	-3.87	34.17	30.70

Finally, the one step transformation of 1,3-bishomocubanone 27 to brendyl system 30, though unanticipated, represents a novel and interesting $C_{10} \rightarrow C_9$ change through a fragmentation - rearrangement sequence. In this context, mention must also be made of fragmentation - recombination products obtained recently from polycyclic ketones, adamantanone[82] (51) and diamantanone[83] (52) during attempted Schmidt reaction

Scheme III.13



51



52

(Scheme III.13). In the light of these results, it seems that Schmidt fission of polycyclic ketones can be a source of many interesting transformations.

III.4 EXPERIMENTAL SECTION

Melting points and boiling points are uncorrected. Melting points were taken in capillaries on a Thomas-Hoover melting point apparatus. Boiling points refer to bath temperature in those cases where short path bulb to bulb distillations were carried out. The petroleum ether corresponds to fraction 60-80°. All solvent extracts were washed with brine and dried over anhydrous sodium sulphate. Infrared spectra were recorded on a Perkin-Elmer Model 137B Spectrophotometer as neat liquids or solids as KBr discs. Pmr spectra were obtained on approximately 10-15% solutions in CCl_4 or $CDCl_3$ on a Varian A-60 spectrometer. The chemical shifts are reported in part per million down field from internal tetramethylsilane at 0.00 as internal standard. The abbreviations s, d, t, q, m and en refer to singlet, doublet, triplet, quartet, multiplet and envelop respectively. Microanalysis were performed by Mr. A.H. Siddiqui in the microanalytical laboratory of our department.

Pentacyclo[5.3.0.$0^{2,5}$.$0^{3,9}$.$0^{4,8}$]decan-6-one[64] (1,3-bishomocubanone, 27)

A solution of endo-dicyclopentadienone (10 g, prepared from dicyclopentadiene, 26, according to the procedure of Woodward and Katz[84]) in cyclohexane (1 l) was purged with a slow stream of purified nitrogen for 30 min. This solution was irradiated in a quartz immersion well with a 450W Hanovia

medium pressure mercury arc lamp for 20 hr. The turbid reaction product containing some suspended polymeric impurities was filtered and the solvent was removed under vacuum to yield 11.5 g of crude product. Filtration of the crude product through a silica gel column (200 g) with 20% benzene-pet ether and direct sublimation (70-80°/10 mm) gave 6.8 g (68% of 1,3-bishomocubanone (27) as a white solid, mp 122-24° (lit.[64] 122-126°).

IR spectrum (KBr): 1750 cm^{-1} (ketone).

PMR spectrum ($CDCl_3$): δ2.23 and 2.42 (-CH-C(=O)-CH, 2H, br, s), 1.68 (H_2C-, 2H, pair of d, J = 12 Hz), 2.7-3.32 (C-H ring, 6H, en).

exo-2-Methanesulphnoxy-9-cyanobrend-4-ene (30)

To a stirred mixture of 1,3-bishomocubanone (27, 1 g, 6.85 mmol) in methanesulphonic acid (6 ml), sodium azide (0.6 g, 9.2 mmol) was slowly added (pinch by pinch) over a period of 30 min. under ice-bath cooling.[85] The dark brown reaction mixture was stirred for an additional hour at ice-bath temp and then poured into ice-water (15 ml). Extraction with methylene chloride (20 ml x 3), washing with 10% sodium carbonate (10 ml x 2) and removal of solvent gave 1.3 g of black solid residue. Filtration through a silica gel (25 g) column, using benzene as an eluent and crystallisation from ether furnished 0.7 g (45%) of mesylate 30 as colourless crystals, mp 88°.

IR spectrum (KBr): 2245 (cyano), 1340, 1175 (mesylate), 945 and 840 cm^{-1}.

PMR spectrum ($CDCl_3$): δ6.20 (olefinic H, 2H, m), 4.60 ($\underline{H}$-$\overset{|}{C}$-OMs, 1H, s), 3.1 ($C\underline{H}_3$-SO_3-, 3H, s), 1.9 ($\underline{H}_2\overset{|}{C}$-, 2H, pair of d, J = 11 Hz), 3.4-2.7 (ring H, 5H, en).

Anal. for $C_{11}H_{13}NO_3S$: Calcd C, 55.21; H, 5.48; N, 5.85.
Found C, 55.04; H, 5.39; N, 5.76.

Hydrogenation of mesylate 30

Mesylate 30 (0.5 g) in ethyl acetate (30 ml), was hydrogenated over 10% Pd/C catalyst at atmospheric pressure (20°). After an uptake of one mol of hydrogen further consumption ceased. The catalyst was filtered off and washed with ethyl acetate. Removal of solvent gave dihydromesylate (31), 0.5 g, in quantitative yield. Recrystallisation from solvent ether furnished needle shaped white crystals, mp 79°.

IR spectrum (KBr): 2240 (cyano), 1330, 1170 (mesylate) and 945 cm^{-1}.

PMR spectrum ($CDCl_3$): δ4.4 ($\underline{H}$-$\overset{|}{C}$-OMs, 1H, s), 3.02 (CH_3-SO_3-, 3H, s), 1.9 (-$C\underline{H}_2$-$C\underline{H}_2$-, 4H, br, s), 1.84 (-$\overset{|}{C}H_2$, 2H, pair of d, J = 11 Hz).

Anal. for $C_{11}H_{15}NO_3S$: Calcd: C, 54.75; H, 6.27; N, 5.80.
Found: C, 54.52; H, 6.14; N, 5.56.

exo-2-Trifluoroacetoxy-9-cyanobrend-4-ene (38)

To a stirred mixture of 1,3-bishomocubanone (27, 1 g, 6.85 mmol) in trifluoroacetic acid (10 ml), sodium azide (0.6 g, 9.2 mmol) was slowly added over a period of 20 min. under ice-bath cooling. The brown reaction mixture was stirred for one more hour at room temp and then poured into ice-water (20 ml). Work-up as described in case of mesylate, yielded 1.4 g of brown viscous residue, which on distillation gave trifluoro-acetate 38, 1.1 g (65%) as a colourless liquid, bp 105-110°/1 mm.

IR spectrum (neat): 2240 (cyano), 1765, 1225 and 1160 cm^{-1} (acetate).

PMR spectrum (CCl_4): δ6.14 (olefinic H, 2H, m), 4.75 ($\underline{H}$-C-O-C-, 1H, s), 1.5 ($\underline{H_2}$C-, 2H, pair of d), 3.7-2.0 (ring H, 5H, en).

Anal. for $C_{12}H_{10}NO_2F_3$: Calcd C, 56.04; H, 3.92; N, 5.45.
Found C, 55.91; H, 3.98; N, 5.39.

exo-2-Hydroxy-9-cyanobrend-4-ene (39)

The ester 38 (1 g) was dissolved in methanol (10 ml) and powdered potassium hydroxide (0.5 g) was added. After stirring for 1 hr at ambient temp the reaction mixture was diluted with water (15 ml) and extracted with ether (20 ml x 3). Washing, drying and evaporation of solvent yielded 0.65 g of crude alcohol 39 . This material was charged on a silica-gel column (20 g) and carefully eluted with benzene to give pure

alcohol (39, 0.35 g, 60%). Distillation furnished a low melting solid, bp 135-40°(bath)/1 mm, mp 44-46°.

IR spectrum (neat): 3475 (hydroxyl), 2245 (cyano), 1045, 850 and 780 cm^{-1}.

PMR spectrum ($CDCl_3$): δ6.11 (olefinic H, 2H, m), 3.75 (H-C-OH, 1H, s), 1.8 (H_2C-, 2H, pair of d, J = 11 Hz), 3.5-2.3 (ring H and -O-H, 6H, en).

Anal. for $C_{10}H_{11}ON$: Calcd C, 74.51; H, 6.88; N, 8.87.
Found C, 74.37; H, 6.92; N, 8.73.

3,5-Dinitrobenzoate of 39 was prepared via reaction with 3:5-dinitrobenzoyl chloride in pyridine according to usual procedure. The 3:5-dinitrobenzoate ester was thus obtained as a light brown crystalline solid, mp 192°.

IR spectrum (KBr): 3040, 2245 (cyano), 1730 (carbonyl), 1620, 1545, 1340 (nitro), 1260, 730 and 720 cm^{-1}.

Anal. for $C_{17}H_{13}N_3O_6$: Calcd C, 57.47; H, 3.67; N, 11.83.
Found C, 57.55; H, 3.86; N, 11.64.

Reaction of alcohol 39 with methanesulphonyl chloride

To an ice-cooled solution of alcohol (0.2 g, 1.24 mmol) in dry pyridine (5 ml), mesyl chloride (0.2 g, 1.75 mmol) was slowly added and the reaction mixture was kept aside for 4 hr. Dilution with ice-water (10 ml), extraction with methylene chloride, followed by washing with 5% HCl and removal of

solvent gave 0.27 g (90%) of mesylate 30. Crystallisation from solvent ether furnished white crystals, mp 88° (mmp 88°). Its ir spectrum was superimposable with the mesylate prepared earlier (vide supra).

9-Cyanobrend-4-en-2-one (40)

A stirred solution of alcohol 39, (0.1 g) in acetone (5 ml) was treated dropwise with Jones reagent[86] (0.5 ml) until the yellow colour persisted. The mixture was stirred for 2 hr, diluted with water and extracted with ether (15 ml x 2). The organic layer was washed with aqueous sodium carbonate, dried and removal of solvent gave 0.065 g (65%) ketone 40. Distillation furnished a colourless liquid, bp 130-135°(bath)/1 mm.

IR spectrum (neat): 2240 (cyano), 1750 cm^{-1} (carbonyl).

2-Cyanotetracyclo[4.3.0.$0^{2,4}$.$0^{3,7}$]non-8-ene (2-cyanodelta-cyclene 41)

To a stirred solution of mesylate (30, 0.5 g, 2.1 mmol) in dry DMSO (10 ml), potassium t-butoxide (0.4 g, 3.6 mmol) was added in one lot. The reaction mixture was warmed to 45° and then stirred for 1 hr. The mixture was poured into ice-water (25 ml) and extracted with ether (20 ml x 2). Washing, drying and evaporation of solvent yilded 0.28 g (95%) of brown oil. Distillation furnished 41 as a colourless liquid, bp 80-85° (bath)/1.5 mm, n_D^{25} 1.5170.

IR spectrum (neat): 3110 (cyclopropyl and olefinic), 2250 (cyano), 855 (tricyclene), 725 and 700 cm^{-1}.

PMR spectrum (CCl_4): δ6.18 (olefinic H, 2H, t, J = 1.5 Hz), 2.9 & 2.75 (allylic H, 2H, s), 1.7 ($-CH_2$, 2H, pair of d, J = 12 Hz), 2.36 (1H, m), 2.13 (1H, s), 1.96 (1H, m).

Anal. for $C_{10}H_9N$: Calcd C, 83.88; H, 6.34; N, 9.78.
Found C, 83.73; H, 6.21; N, 10.01.

2-Cyanodeltacyclane (44)

To a stirred solution of dihydromesylate (31, 0.5 g, 2.1 mmol) in dry DMSO (10 ml) potassium t-butoxide (0.4 g, 3.6 mmol) was added in one lot and then warmed upto 45°. After 1 hr the reaction mixture was poured into ice-water (20 ml) and extracted with ether. Removal of ether yielded 0.285 g (95%) of crude product. Direct distillation furnished 44 as a colourless oil, bp 80-85°(bath)/1 mm.

IR spectrum (neat): 3075 (cyclopropane), 2225 (cyano), 1450, 855 (tricyclene), and 785 cm^{-1}.

PMR spectrum (CCl_4): δ 2.24 (1H, s), 2.12 (1H, s), 1.72 (9H, en).

Anal. for $C_{10}H_{11}N$: Calcd C, 82.72; H, 7.64; N, 9.65.
Found C, 82.81; H, 7.70; N, 9.86.

2-Cyanopentacyclo[4.3.0.$0^{2,4}$.$0^{3,8}$.$0^{5,7}$]nonane (45)

A solution of 2-cyanodeltacyclene (41, 0.2 g) in acetone (150 ml) was purged with a slow stream of purified nitrogen for 20 min. The solution was then irradiated with a 450 W, Hanovia medium pressure mercury arc lamp using Vycore 521 filter for 2 hr. Removal of solvent and filtration through a small silica gel column (10 g), yilded 0.14 g (70%) of oily residue. Sublimation of the product at 60°/15 mm furnished 45 as a low melting solid, mp 46-50°.

IR spectrum (neat): 3070 (cyclopropane), 2240 (cyano) and 855 cm^{-1}.

PMR spectrum (CCl_4):δ2.24 (1H, s), 2.12 (1H, s), 1.74 (5H, m), 1.24 (2H, s).

Anal. for $C_{10}H_9N$: Calcd C, 83.88; H, 6.34; N, 9.78.
Found C, 83.71; H, 6.42; N, 9.54.

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CHAPTER IV

REGIOSPECIFIC BAEYER-VILLIGER OXIDATION OF POLYCYCLIC KETONES WITH CERIC ION

IV.1 ABSTRACT

Efficient and preparatively useful Baeyer-Villiger oxidation of a few strained polyclic ketones with ceric ion is reported. Oxidation of pentacyclo[5.3.0.$0^{2,5}$.$0^{3,9}$.$0^{4,8}$]decan-6-one (1,3-bishomocubanone, 20), pentacyclo[5.3.0.$0^{2,6}$.$0^{3,9}$.$0^{4,8}$]-decan-5-one (1,4-bishomocubanone, 21) and pentacyclo-[6.2.1.$0^{2,7}$.$0^{4,10}$.$0^{5,9}$]undecan-3,6-dione (22) with ceric ammonium nitrate (CAN) or ceric ammonium sulphate (CAS) furnishes the corresponding lactones (31), (44) & (45) in good yield . For comparison, peracid oxidation of ketones 20, 21 and 22 has also been investigated. Structures of all the lactonic products 31, 32, 44, 45, & 49 have been deduced from complimentary spectral data and chemical degradation. The BV oxidation of unsymmetrical 1,3-bishomocubanone (20) & dione (22) proceeds regiospecifically and the results differ from those of conventional peracid oxidation. This observation

may be of general synthetic utility in carrying out regiospecific BV oxidation of geometrically constrained polycyclic ketones with ceric ion. A plausible mechanism has been advanced to explain the regiospecificity of ceric ion oxidations.

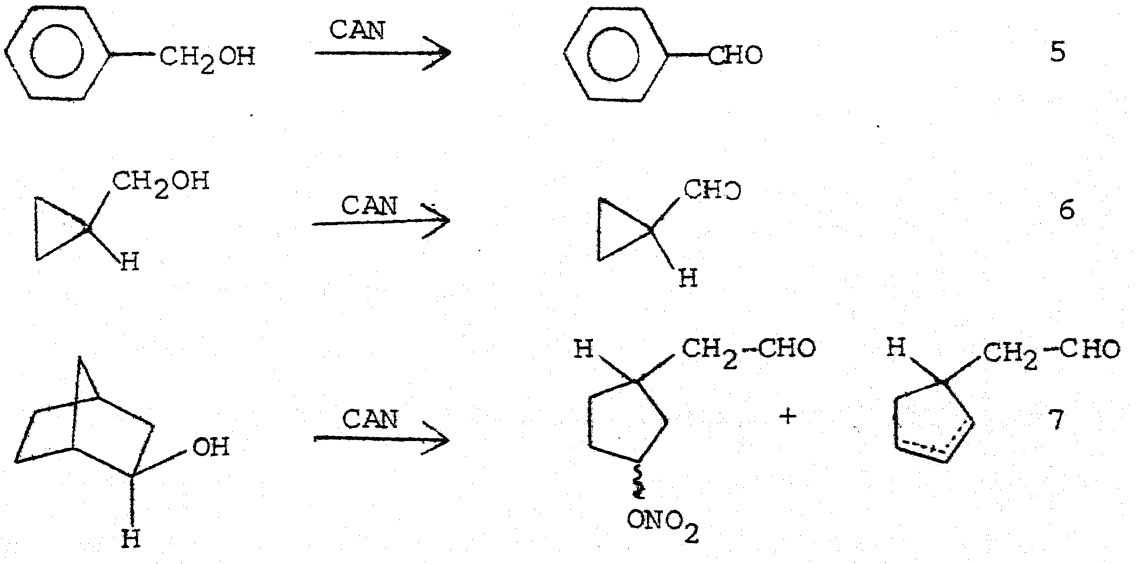
IV.2 INTRODUCTION

Ceric ion in various coordinated forms has been known as a strong oxidising agent for many decades.[1] However, early use of ceric ion in organic chemistry was primarily restricted to colorimetric and quantitative estimation[2] of alcohols. Later studies revealed the ability of ceric ion to oxidise a variety of organic functional groups but these efforts were mostly devoted to the elucidation of reaction kinetics and little, if any, effort was expended to the preparative aspects of these reactions.[1] Investigations during the last decade by Trahanovsky[3] and others[4] on ceric ammonium nitrate (CAN) and ceric ammonium sulphate (CAS) oxidation of a number of organic compounds have drawn attention to the synthetic versatility of ceric ion in preparative organic chemistry.[4] Consequently, a great deal of promising synthetic methodology has been realised[4] employing ceric ions. As the results described in this chapter deal with a novel preparative aspect of ceric ion oxidation, it will be desirable to briefly discuss the oxidation of common organic functional groups with ceric reagents.

ALCOHOLS

Among the various functional groups, alcohols are most readily oxidised by ceric ion and their reactions have been extensively studied. Thus, benzylic[5] and cyclopropylcarbinyl[6] alcohols are oxidised to the corresponding aldehydes. Bridged bicyclic alcohols[7] and cyclobutanols[8] are oxidised with adjascent C-C bond fission. α-Glycols are cleaved[9] by ceric ion and alkanols possessing a δ-hydrogen atom, such as n-pentanol,[10] produce tetrahydrofuran derivatives in analogy with lead tetraacetate oxidations. Simple cyclic alcohols like cyclopentanol and cyclohexanol as well as adamantanol are dehydrogenated[11] to the corresponding ketones in the presence of ceric ion. These reactions with typical illustrations are depicted in Scheme IV.1. Mechanistic studies[8,12] have suggested that ceric ion-induced alcohol cleavage is a one electron process, whereas for ketone formation a two electron oxidation is operative.

Scheme IV.1



Ref.

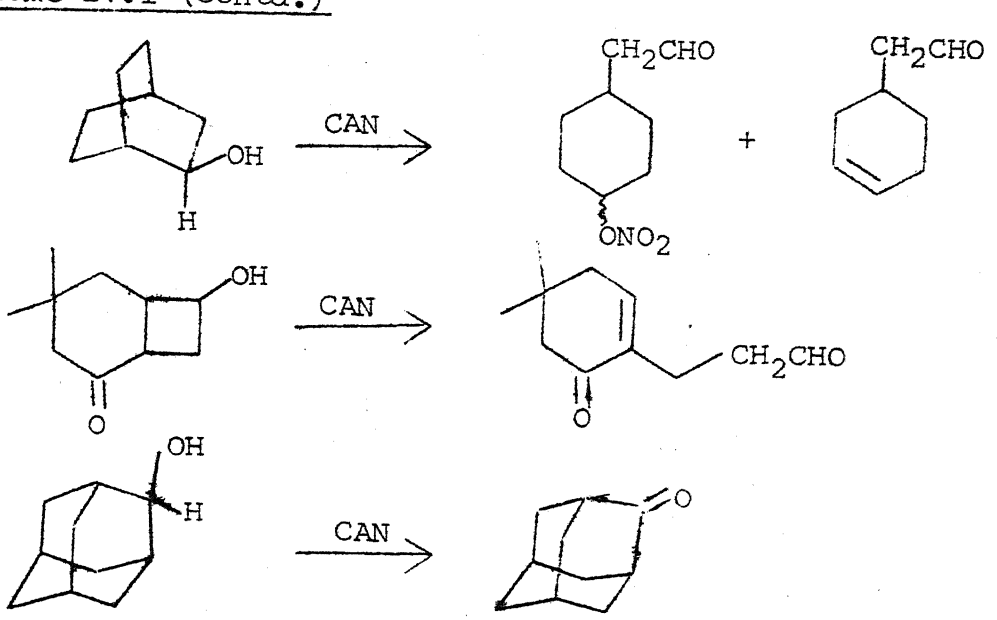
5

6

7

contd.

Scheme IV.1 (contd.)



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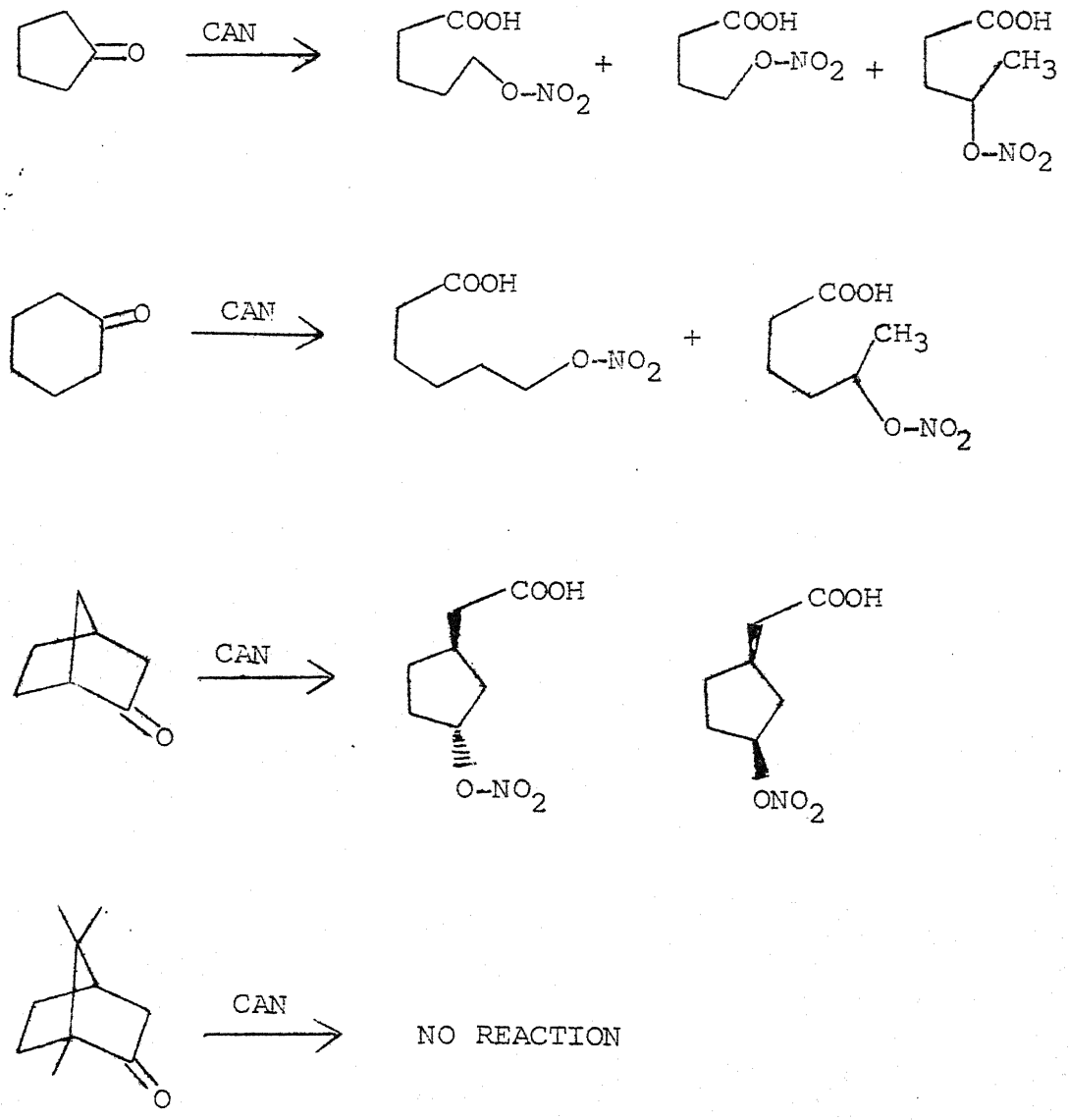
8

11

CARBONYL COMPOUNDS

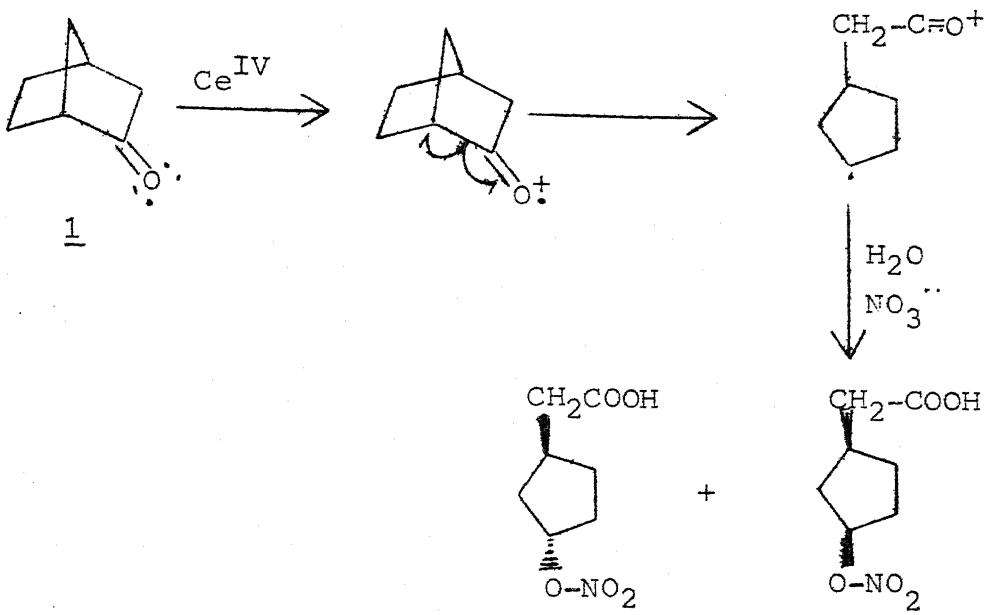
Alicyclic ketones are rapidly consumed by ceric ammonium nitrate or ceric ammonium sulphate to furnish corresponding ω-nitratocarboxylic acids via a pathway involving α-cleavage.[13] Cyclopentanone, cyclohexanone and norbornanone (1) belong to this category and furnish mixtures of ring opened carboxylic acids (Scheme IV.2). Surprisingly, camphor is inert towards CAN and this indicates that these oxidations require a close approach of the ketone and ceric ion, perhaps a complex formation is involved. Since, Ce^{+4} is a bulky species in solution due to coordination with 8 to 12 atoms, its approach to camphor carbonyl is prohibited. Several mechanisms involving an enol intermediate[14] as well as α-hydrogen abstraction[15] have been formulated for ceric ion oxidation of ketones. Unfortunately, these proposals are mainly derived from kinetic data and are

Scheme IV.2



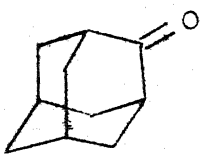
not backed up by detailed product analysis. The currently accepted mechanism[4,13] of ketone oxidation is illustrated in Scheme IV.3 for 2-norbornanone (1) oxidation.

Scheme IV.3



1

Adamantanone (2) and tetracyclone (3) exhibit unexpected behaviour towards CAN and undergo efficient Baeyer-Villiger oxidation[13,16] to the lactone (4) and tetraphenyl α-pyrone (5), respectively.



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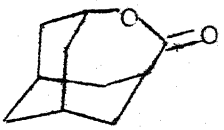

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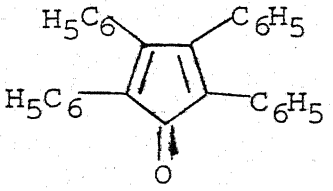
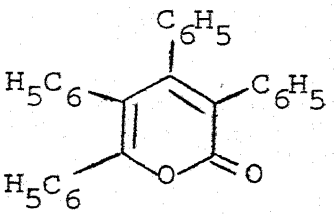


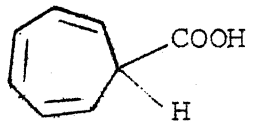
3



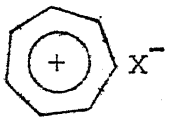
5

CARBOXYLIC ACIDS

Simple aliphatic and aromatic carboxylic acids are usually stable towards ceric ion. However, oxalic acid[17] and malonic acid[18] are readily oxidised by ceric ion to carbon dioxide and water. The higher homologues of these dicarboxylic acids do not react with ceric ion. Cycloheptatriene carboxylic acid (6) is readily decarboxylated to tropylium salt (7) with CAN in 30% yield.[19]



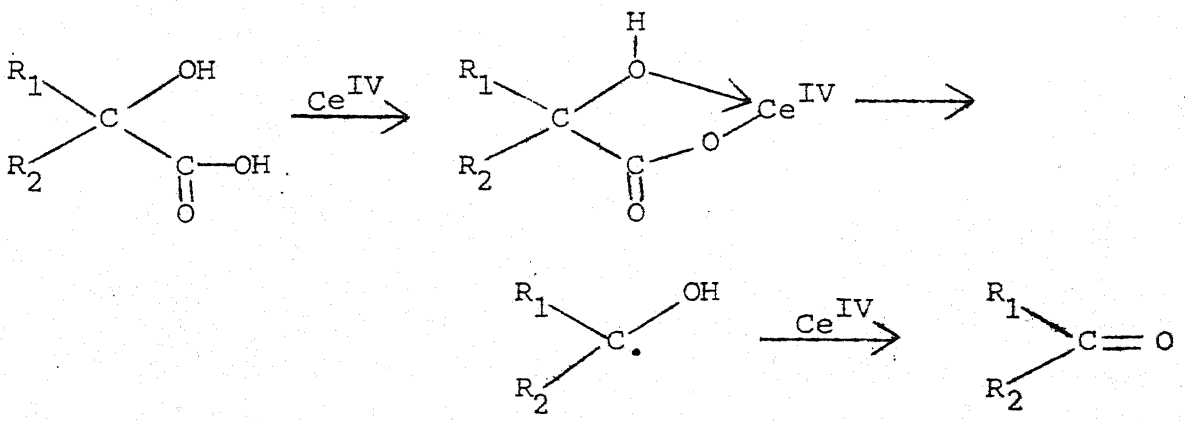
6



7

α-Hydroxycarboxylic acids are degraded[20] to carbonyl compounds with the loss of a carbon atom by ceric ion and this constitutes a useful degradative method (Scheme IV.4):

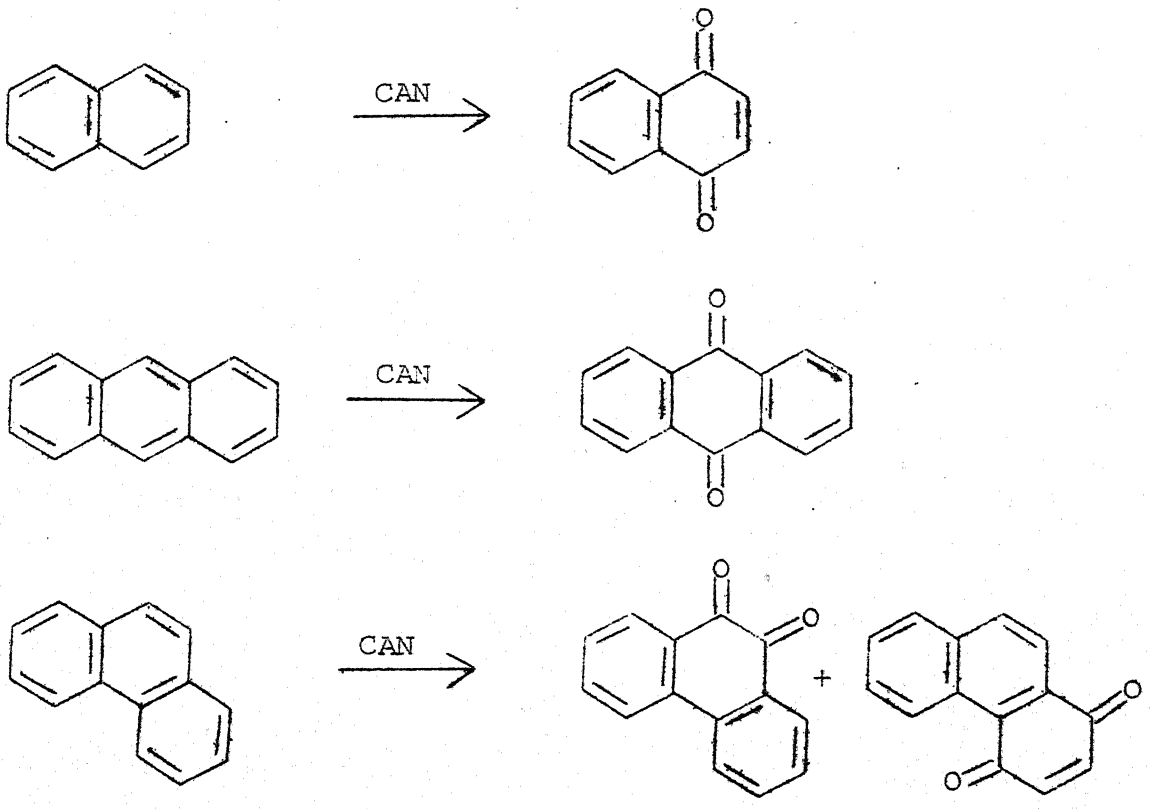
Scheme IV.4



HYDROCARBONS

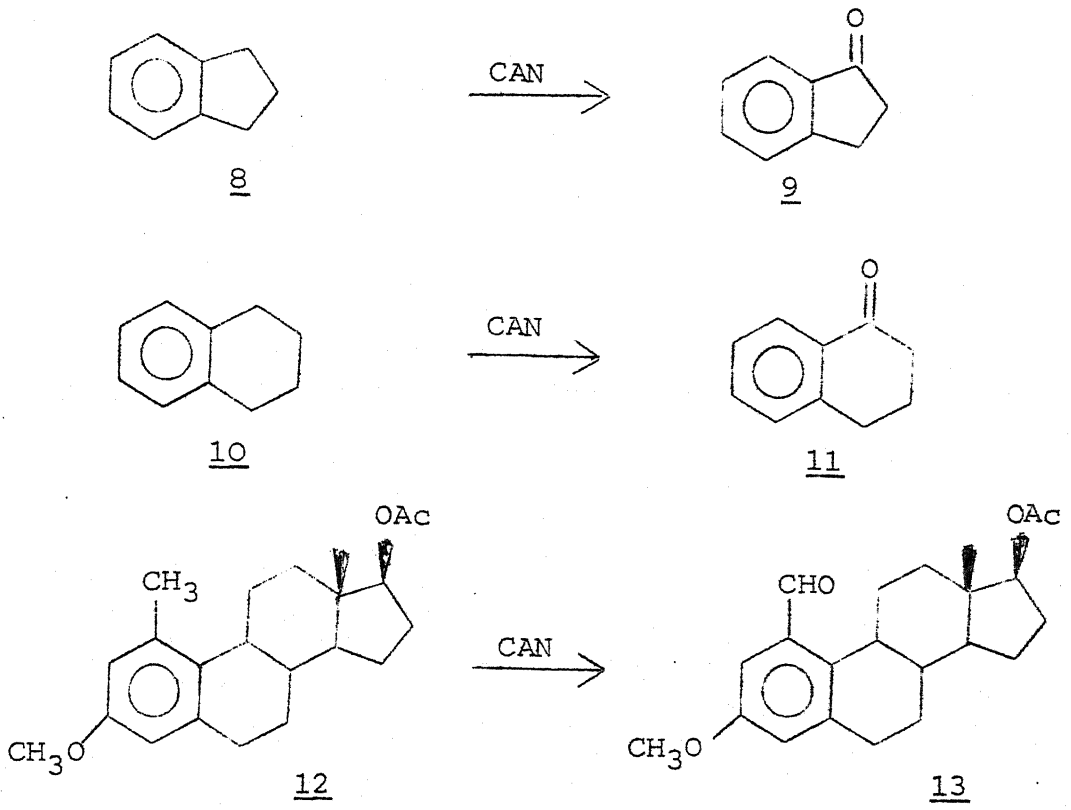
Aromatic hydrocarbons possessing benzylic methyl and methylene groups are rapidly oxidised to corresponding carbonyl functions by CAN in acidic medium.[21] Thus, o- and p-xylenes are oxidised to 2- and 4-methyl benzaldehydes respectively in 100% yield.[21] Polynuclear hydrocarbons are directly oxidised[22] to quinones by CAN under mild conditions are in reasonable yields (Scheme IV.5).

Scheme IV.5



Efficient conversion of indane (8) to 1-indanone (9) tetralin (10) to 1-tetralone (11) and steroidal[23] substrate 12 to 13 are useful examples of hydrocarbon oxidation (Scheme IV.6):

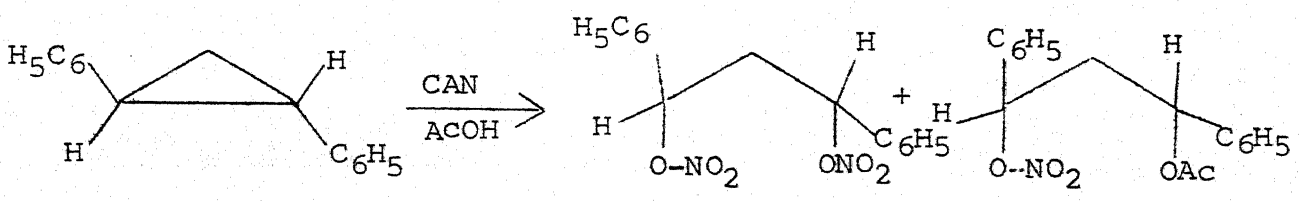
Scheme IV.6



8 9 10 11 12 13

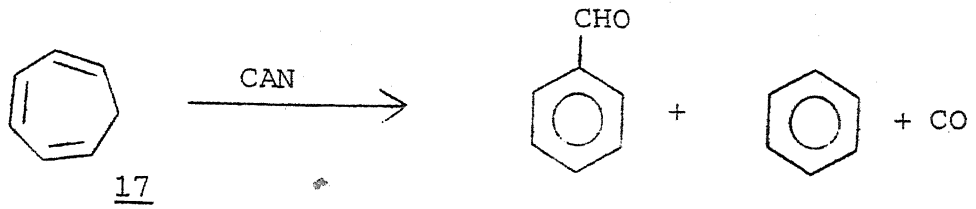
Aryl cyclopropanes like 14 are cleaved[24] by CAN in acetic acid to ring opened products 15 and 16 (Scheme IV.7). A mechanistically interesting example[25] of hydrocarbon oxidation is the oxidation of cycloheptatriene (17) to benzaldehyde, benzene and carbon monoxide (Scheme IV.8):

Scheme IV.7



14 15 16

Scheme IV.8

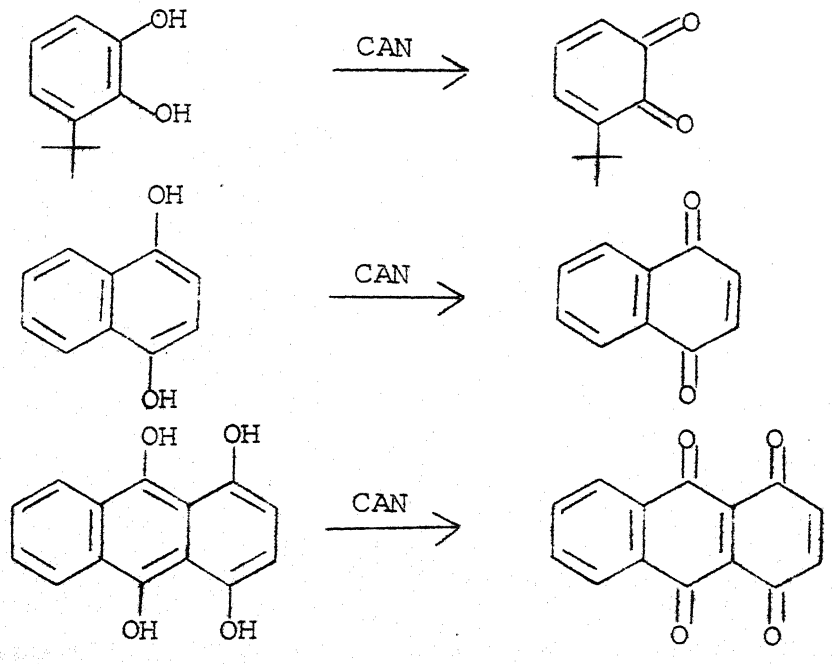


17

HYDROQUINONES

Oxidation of hydroquinones to quinones can be effected with a variety of reagents but these reactions are generally messy and handicapped by low yields. However, hydroquinones can be rapidly and efficiently oxidised[26] to the corresponding quinones by CAN. This oxidation procedure is applicable for the generation of ortho-, para- and diquinones (Scheme IV.9):

Scheme IV.9



OXIMES AND SEMICARBAZONES

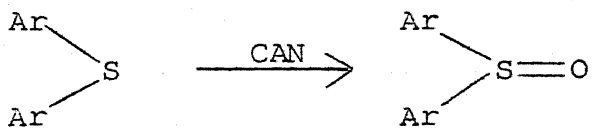
In many synthetic operations, it is expedient to either protect or purify carbonyl compounds via their oxime and

semicarbazone derivatives. Ceric ammonium nitrate regenerates[27] the parent ketone or aldehyde from oximes and semicarbazones at low temperature and in good yields. Thus providing a superior and mild alternative to the conventionally used regeneration procedures.[27]

MISCELLANEOUS

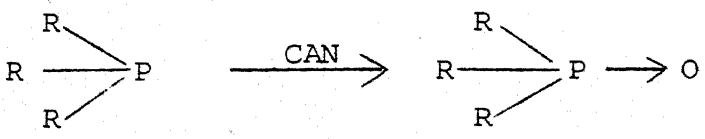
Diaryl sulphides are readily oxidised to the corresponding sulphoxides in high yield without any contamination of corresponding sulphones[28] (Scheme IV.10). Similarly, phosphines

Scheme IV.10



are quantitatively oxygenated[16] to phosphine oxides by ceric ion (Scheme IV.11). Lastly, ceric ions facilitate elimination

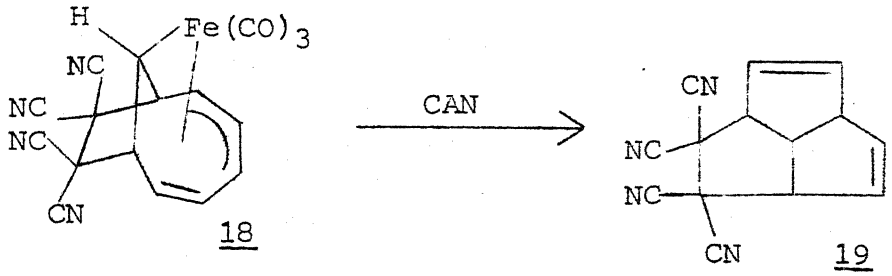
Scheme IV.11



of π-ligands from organometallic complexes. For example, convenient release[29] of cyclobutadiene from the cyclobutadiene-iron tricarbonyl complex with ceric ion paved the way for its various synthetic applications.[30,31] Several analogous reactions are

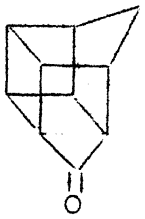
reported in literature.[32,33] A fascinating example[34] is the generation of triquinacene framework 19 from iron tricarbonyl complex 18 with CAN (Scheme IV.12):

Scheme IV.12

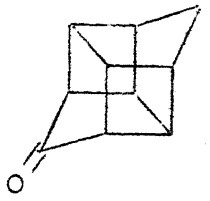


18 19

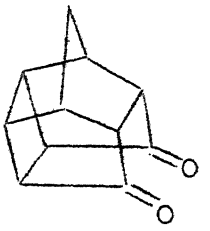
In pursuit of certain synthetic objectives, it became necessary to carry out Baeyer-Villiger (BV) oxidation of pentacyclo[5.3.0.0^{2,5}.0^{3,9}.0^{4,8}]decan-6-one (1,3-bishomocubanone, 20).[35] Although, m-chloroperbenzoic acid or related peracid would be the obvious reagent for accomplishing this transformation, the relative simplicity and high yield of oxidation[13] of adamantanone (2) to lactone (4) with ceric ammonium nitrate encouraged us to employ this reagent for the Baeyer-Villiger oxidation of 20. The realisation of facile BV oxidation of 1,3-bishomocubanone, (20), vide infra, prompted us to extend the scope of this synthetic reaction to two other polycyclic ketones, pentacyclo[5.3.0.0^{2,6}.0^{3,9}.0^{4,8}]decan-5-one (1,4-bishomocubanone, 21)[36] and pentacyclo[6.2.1.0^{2,7}.0^{4,10}.0^{5,9}]undecan-3,6-dione (22).[37] All three polycyclic ketones 20, 21 and 22 have been found to undergo efficient BV oxidation with CAN or CAS. Furthermore, the oxidation of unsymmetrical 1,3-bishomocubanone (20) and pentacyclic dione (22) proceeds in a highly regiospecific manner to furnish lactones different



20



21



22

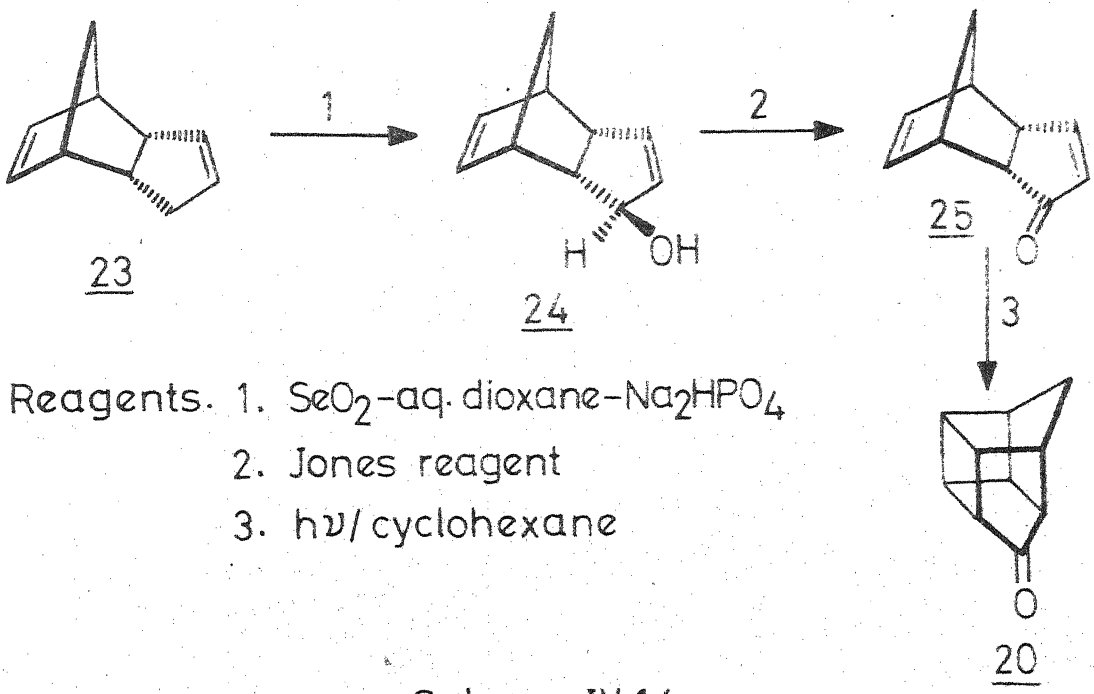
from those obtained by the conventional peracid oxidation.

In this chapter of the thesis, results of reaction of ketones 20, 21 and 22 with ceric ammonium sulphate, ceric ammonium nitrate and m-chloroperbenzoic acid are described. The results highlight the preparative role of ceric reagents (CAN & CAS) in carrying out regiospecific BV oxidation of geometrically constrained multicyclic ketones. A plausible mechanism is advanced to explain the regiospecificity of ceric ion oxidations.

IV.3 RESULTS AND DISCUSSION

The three polycyclic ketones, 1,3-bishomocubanone (20), 1,4-bishomocubanone (21) and pentacyclic dione (22) were readily assembled according to literature procedures[35-37] with slight modification of experimental conditions. 1,3-Bishomocubanone (20) was prepared[35] from readily available dicyclopentadiene (23) and involved an intramolecular $\pi 2_s + \pi 2_s$ photoaddition of dicyclopentadienone 25 as the key step. The synthetic sequence leading to 20 from dicyclopentadiene (23) is depicted in Scheme IV.13.

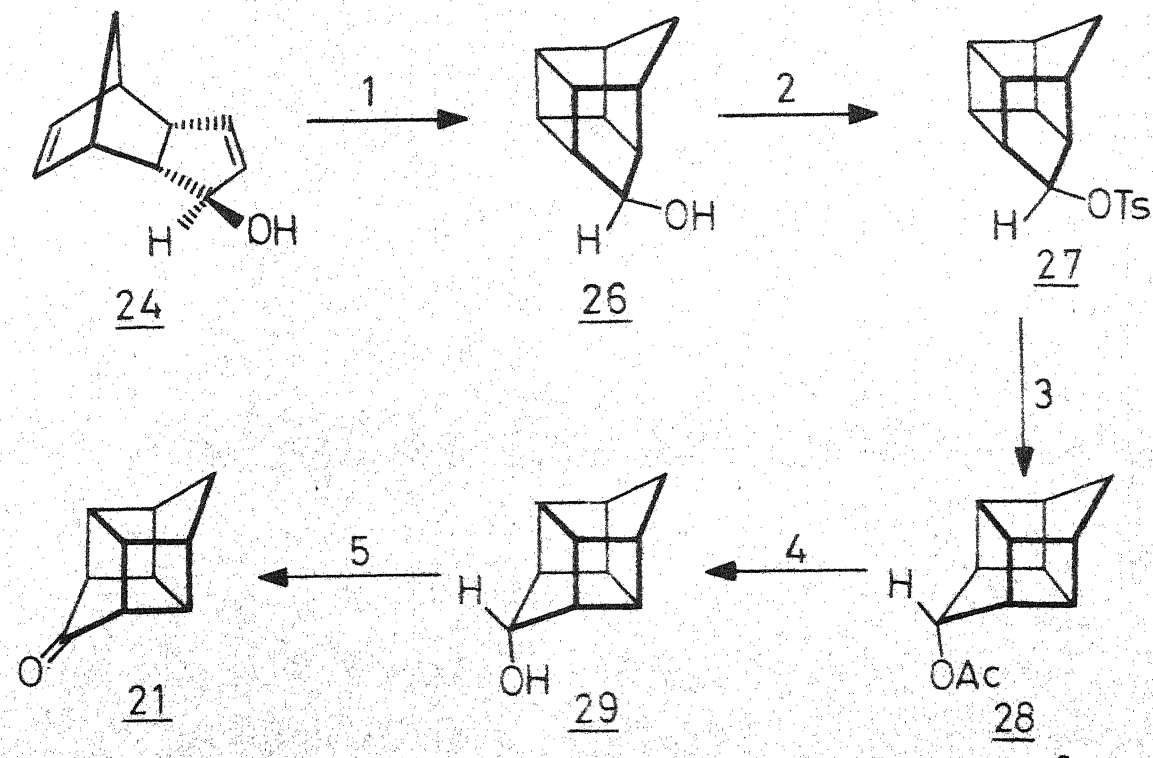
Scheme IV.13



23 24 25 20

Reagents. 1. SeO_2-aq. dioxane-Na_2HPO_4
2. Jones reagent
3. hν/ cyclohexane

Scheme IV.14



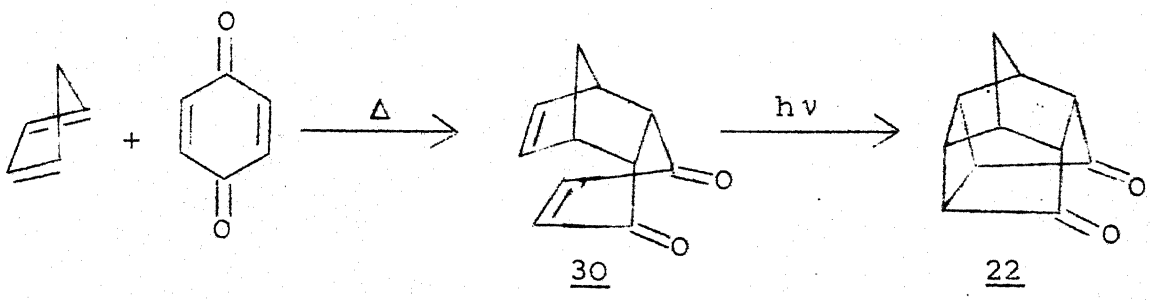
24 26 27 28 29 21

Reagents. 1. hν/acetone 2. TsCl/Py 3. AcOH,120°
4. $LiAlH_4$-Et_2O 5. Jones reagent

1,4-Bishomocubanone (21) was prepared[36] from anti-1,3-bishomocubanol (26) involving a solvolytic Wagner-Meerwein type of rearrangement. Thus, unbuffered acetolysis of tosylate (27) furnished the rearranged acetate (28) which after reduction with lithium aluminium hydride to 1,4-bishomocubanol (29) was directly oxidised to 1,4-bishomocubanone (21). The pentacyclic alcohol (26) was prepared from dicyclopentadiene (23) via the acetone sensitised photochemical ring closure of endo-,anti-tricyclo[5.2.1.$0^{2,6}$]deca-4,8-dien-3-ol (24). The entire reaction secuence from dicyclopentadiene (23) to 1,4-bishomocubanone (21) is summarised in Scheme IV.14.

The pentacyclic dione (22) was easily constructed[37] from cyclopentadiene-p-benzoquinone adduct (30) through intramolecular $\pi 2_s + \pi 2_s$ photoaddition (Scheme IV.15):

Scheme IV.15

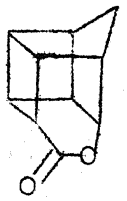


30 22

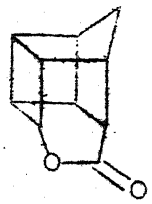
All the three starting ketones 20, 21 & 22 exhibited infrared, pmr and melting points entirely consistent with the values reported in literature.[35-37]

Reaction of 1,3-bishomocubanone (20) with a slurry of ceric ammonium sulphate (CAS) or ceric ammonium nitrate (CAN) in aq. acetonitrile furnished a single product, mp 133-5°, in 78% yield. Mass spectral measurements (M^+ 162) and strong

infrared absorptions at 1760, 1180 and 1000 cm^{-1} suggested a δ-lactone (boat)[38-40] structure for the product. This contention was clearly supported by the pmr spectrum (Fig. IV.1) which displayed a 1H quartet at 5.05 (J_1 = 4 Hz and J_2 = 3 Hz) due to the presence of a H-C(-O)-O-C(=O)- type proton and mass spectral peaks at m/e 118 ($M^+ - CO_2$) and 117 ($M^+ - CO_2H$). This data is compatible with either structure 31 or 32 for the CAS oxidation product.



31



32

At this stage, in order to confirm that the ceric ion oxidation product was indeed a BV product, peracid oxidation of 20 was investigated. When 20 was reacted with m-chloroperbenzoic acid, a 5:1 mixture of two lactones was obtained. The major compound (M^+ 162), mp 145-6°, showed typical δ-lactone (boat)[38-40] bands at 1755 & 1070 cm^{-1} and was distinctly different from the lactone obtained *via* CAS oxidation of 20. Its pmr spectrum (Fig. IV.2) as expected, showed a triplet at δ4.71 (J= 6 Hz) due to a H-C(-O)-O-C(=O)- type proton. This data was suggestive of either structure 31 or 32 for the lactone. The minor product from the peracid oxidation, however, proved to be identical with the lactone obtained from CAS oxidation. The pmr data for the two lactones, particularly the

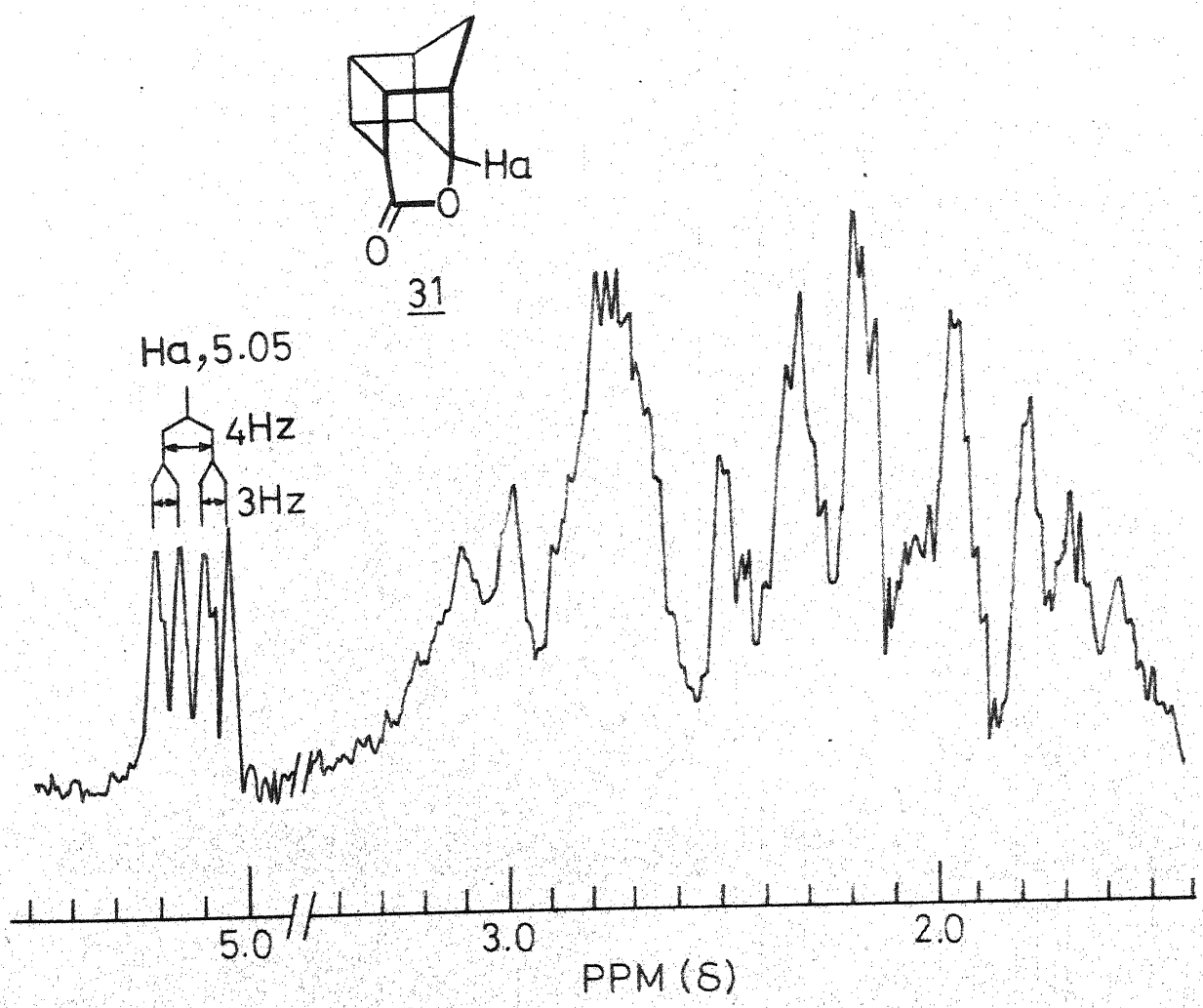
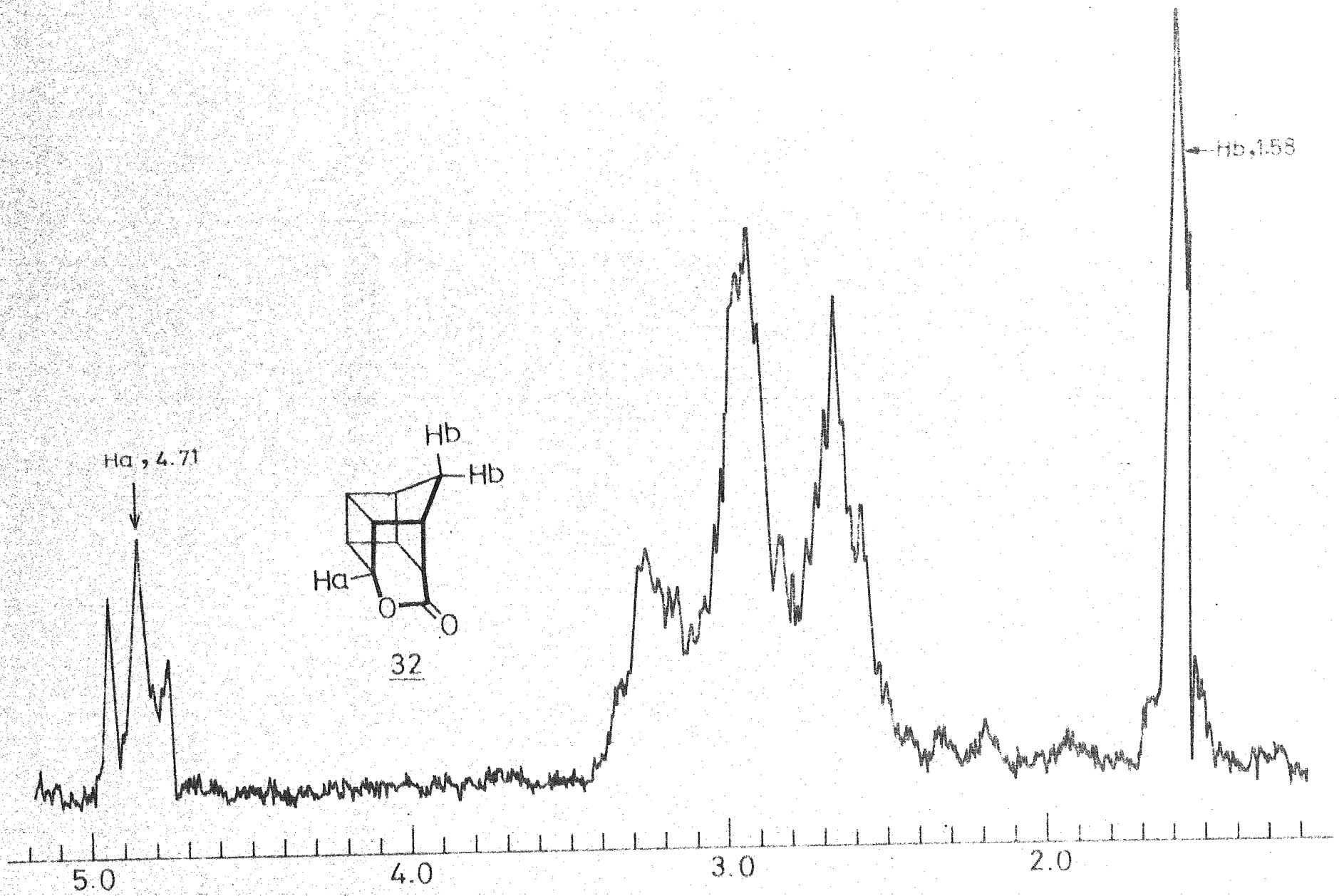


Fig. IV. 1 PMR spectrum (60 MHz) of 31



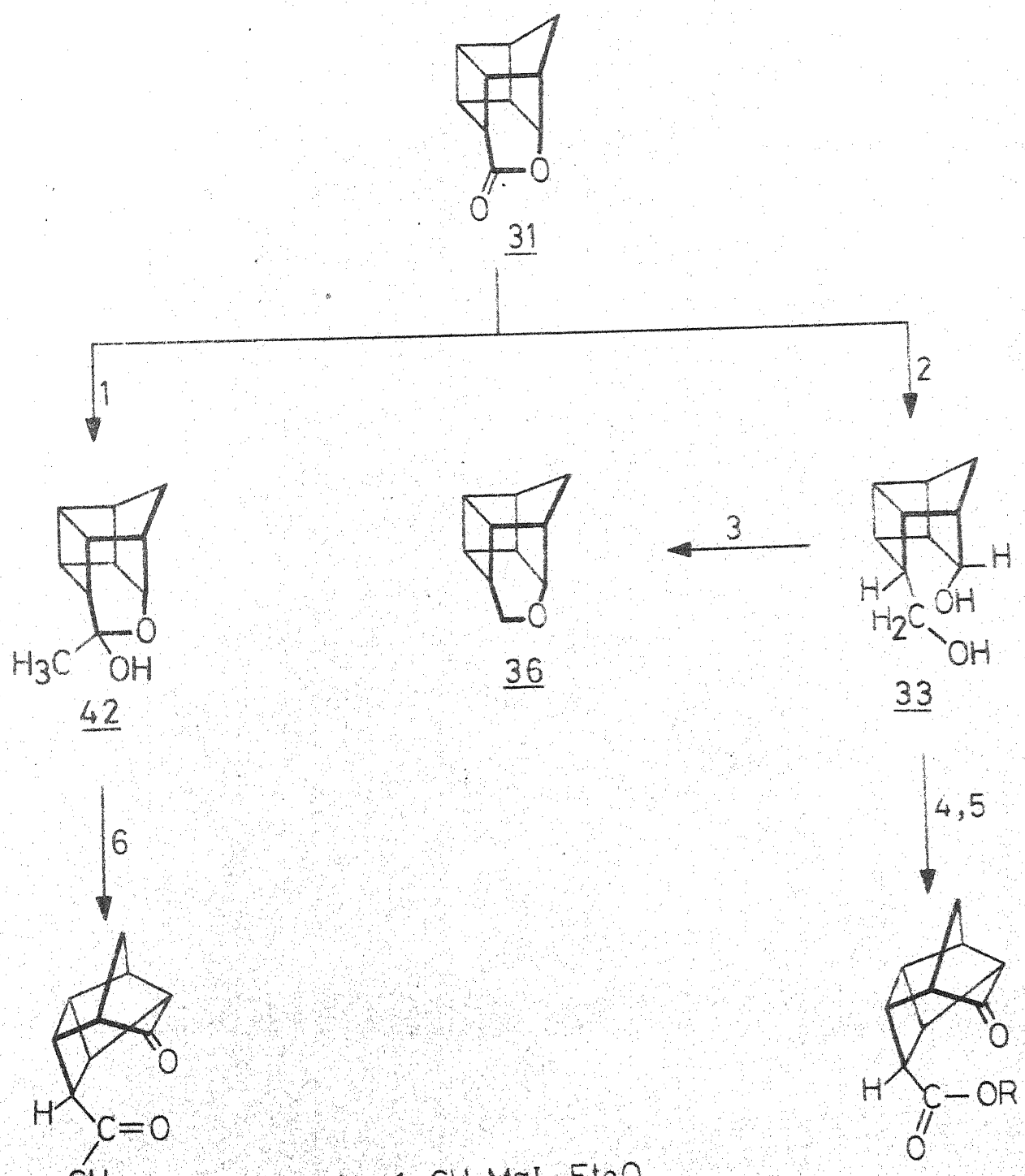
32

Fig. IV. 2 PMR spectrum (60 MHz) of 32

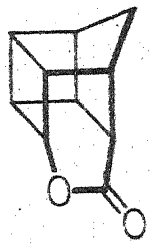
multiplicity of the low field signal, was strongly indicative of their being positional isomers 31 & 32 but was of little diagnostic value in distinguishing them. The possibility of any skeletal rearrangement was ruled out on the basis of the mass spectral fragmentation which showed strong peaks at m/e 66 ($C_5H_6^+$) diagnostic[41,42] of this system and resulting from the cleavage of the carbon skeleton in half. Strong peak at m/e 91 ($C_7H_7^+$) attributed[41,42] to tropylium ion was also observed in all of these compounds. A degradative scheme was therefore designed to elucidate the structures of the two lactones. It may be mentioned here that attempted base hydrolysis or methanolysis of lactones (31) & (32) always oed to quantitative recovery of the starting material and therefore a more circuitous degradative scheme was selected (Scheme IV.16 & IV.17).

The CAS lactone was reduced by lithium aluminium hydride to the diol (33), mp 125°, and oxidised with Jones reagent to the keto acid (34). Diazomethane esterification of 34 gave the keto ester (35) which displayed ir absorptions at 1750 (cyclopentanone) and 1730 (ester) cm^{-1} along with expected pmr resonances and established the structure of this lactone as 31. Analogous reduction of peracid lactone with lithium aluminium hydride did not furnish any diol and only a crystalline pentacyclic ether (37), mp 192°, was obtained. The structure of this ether (37) follows from mass spectral measurements (M^+ 148), ir spectrum (strong bands at 1025 & 955 cm^{-1}) and pmr spectrum

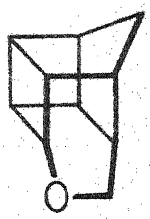
Scheme IV.16


31
1
2
3
42
36
33
4,5
6
34 R = H
35 R = CH3
43
Reagents: 1. CH3MgI – Et2O
2. LiAlH4 – Et2O
3. pTs A – Benzene
4. Jones Reagent
5. CH2N2 – Et2O
6. Jones Reagent

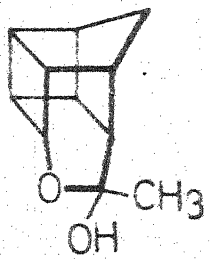
Scheme IV.17



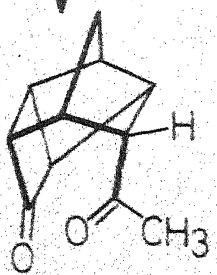
32



37



40



41

Reagents : 1. $LiAlH_4-Et_2O$

2. $CH_3MgI-Et_2O$

3. Jones reagent

(Fig. IV.3) which exhibited a 1H multiplet centred at δ5.52 and 2H triplet centred at δ 4.13 (J= 5 Hz) ascribable to $\underline{H}\text{-}\overset{|}{C}\text{-}O\text{-}\overset{|}{C}\underline{H}_2$ type of functionality. The rest of the spectrum consisted of a broad envelop between δ 1.3-3.3 due to remaining ring protons. For comparison, an isomeric ether (36), mp 140°, was also prepared from diol (33) by dehydration with p-toluenesulphonic acid in refluxing benzene. The ether (36) (M^+ 148), as expected, exhibited pmr signals (Fig. IV.4) at δ 4.8 (1H, m) and δ 4.0 (2H, m) due to $\underline{H}\text{-}\overset{|}{C}\text{-}O\text{-}\overset{|}{C}\underline{H}_2$ type of functionality. However, a distinction between isomeric ethers (36) & (37) could not be achieved on spectral grounds.

The difference in reactivity of LAH towards isomeric lactones (31) & (32) leading to the formation of diol (33) and ether (37) respectively was quite unanticipated. However, to rationalize the different behaviour of 31 and 32 towards lithium aluminium hydride, a tentative suggestion may be made. In the structures (38 & 39) of the reduction products before work-up, the substituents (H, OX in 38 and H, CH_2OX in 39) would be displaced to a slight extent by twisting (cf. arrows) in order to minimize steric strain. This action as well as the tilting of the carbon atoms bearing these substituents upward are favoured by the presence of the bond indicated in bold-type. For ether formation from 38, the OX of the CH_2-OX (X = H or Al$<$) group must swing inward the molecular cavity in order to attain a good S_N2 transition state[43] and it is strongly opposed by steric interactions. On the other hand,

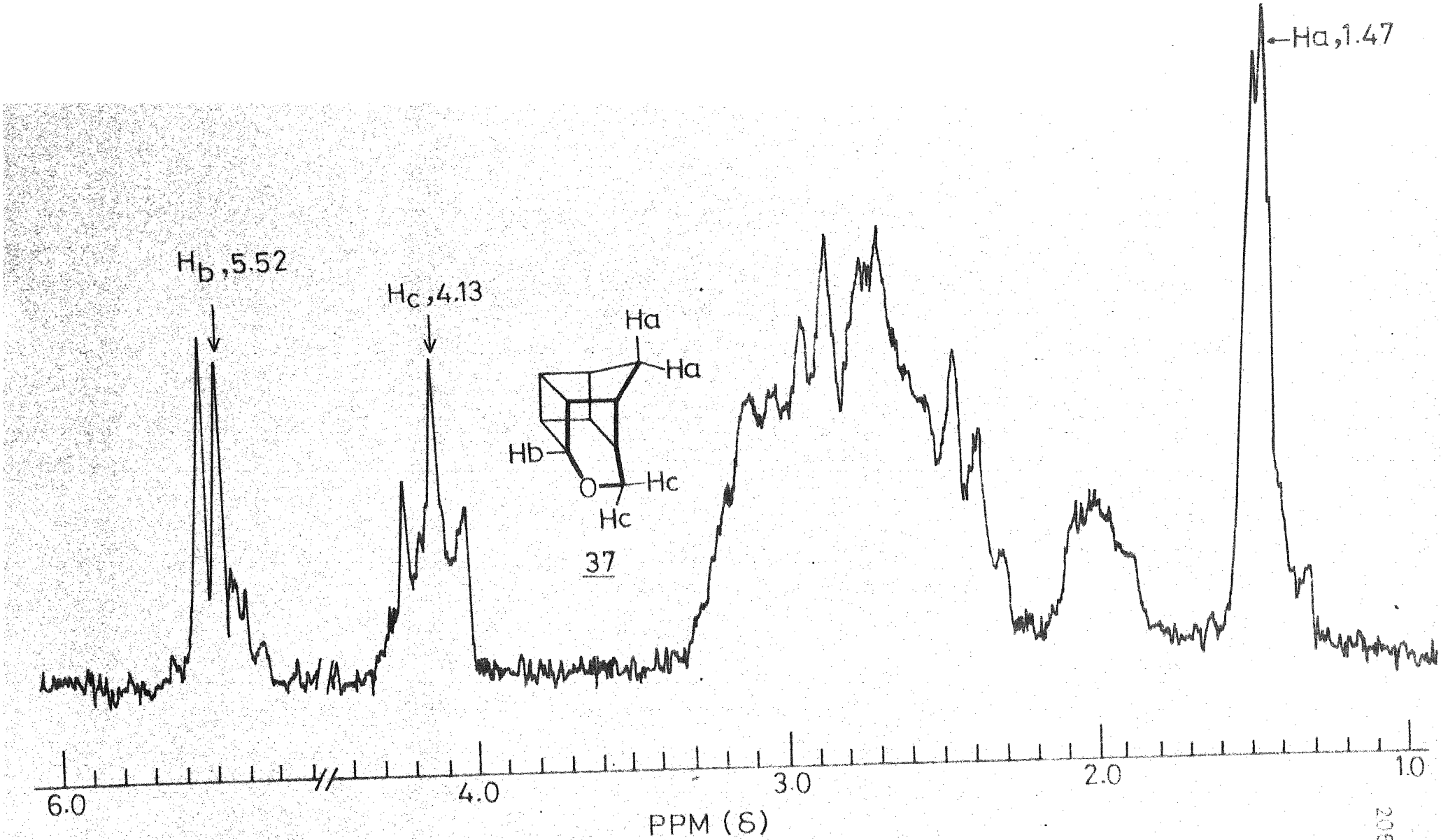
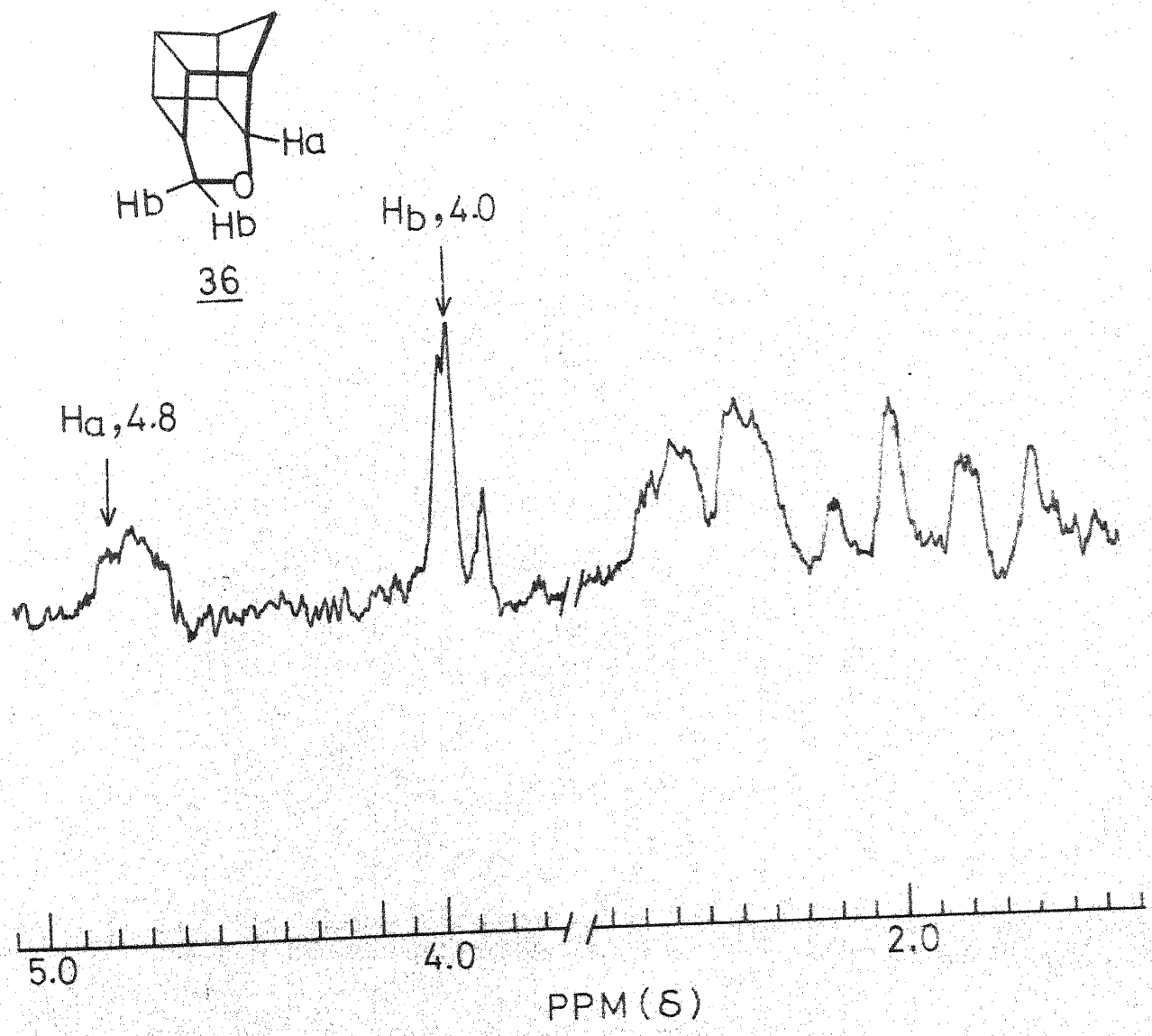


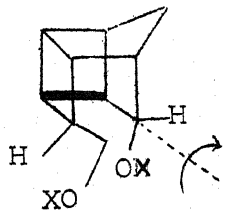
Fig. IV.3 PMR spectrum (60 MHz) of 37



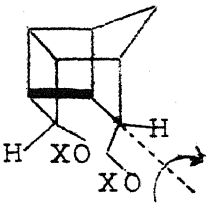
36

Fig. IV.4 PMR spectrum (60MHz) of 36

the deformation of 39 tends to align the attacking and the leaving groups in a better disposition for ether formation.

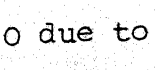


38



39

Addition of methylmagnesium iodide to the peracid lactone (32) yielded the lactol (40, ir: 3550, 1050, 1055 cm^{-1} and pmr: δ1.38,3H, singlet), which was oxidised with Jones reagent to the diketone (41) exhibiting cyclobutanone absorption (1775 cm^{-1}) in the ir spectrum. Analogous degradation of CAS lactone *via* the lactol (42, ir: 3500, 1010, 1050 cm^{-1} and pmr: δ 1.6 3H, singlet) yielded the isomeric diketone (43) displaying a cyclopentanone absorption (1740 cm^{-1}). The structure of Ce^{+4} and peracid lactones were thus established as 31 and 32 respectively.

The symmetrical 1,4-bishomocubanone (21) on CAS oxidation furnished a crystalline lactone (44), mp 130-32°, which showed ir bands at 1755 & 1260 cm^{-1} (δ-lactone)[38-40] and a proton at δ5.0 due to  type functionality (Fig. IV.5). The same lactone was also obtained from the peracid oxidation of 21.

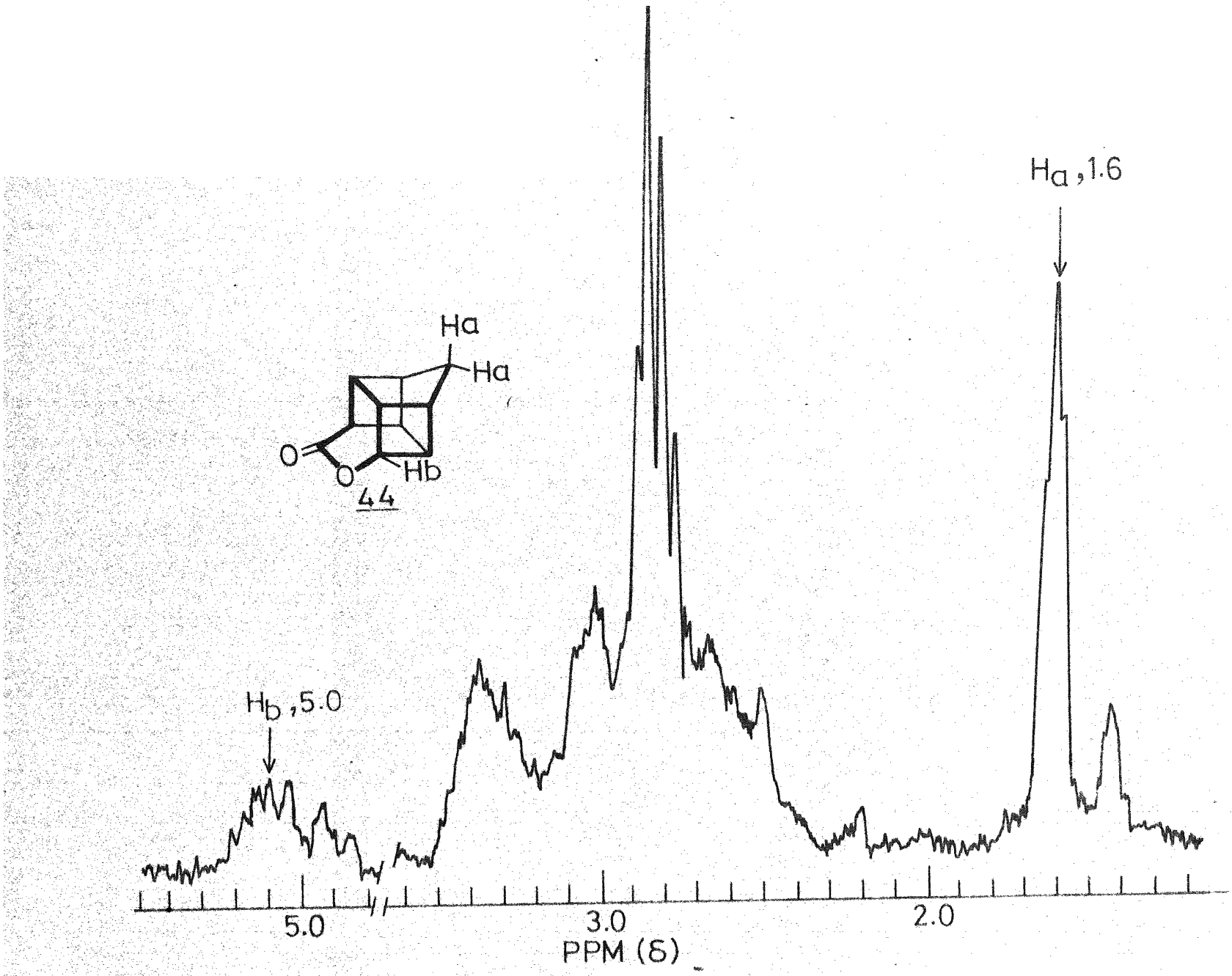
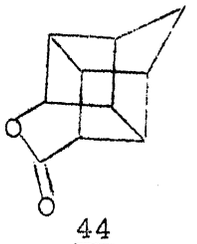
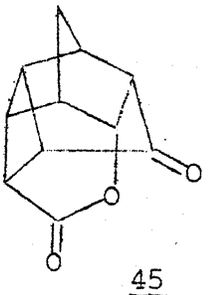


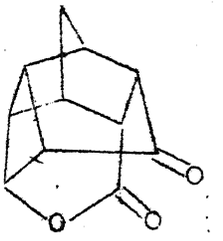
Fig. IV. 5 PMR spectrum (60 MHz) of 44



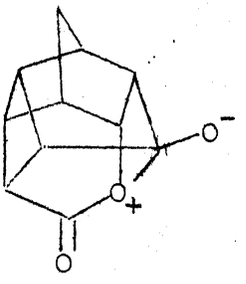
44



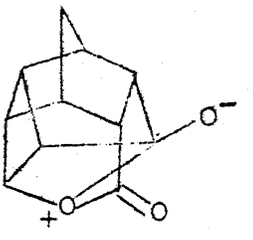
45



46

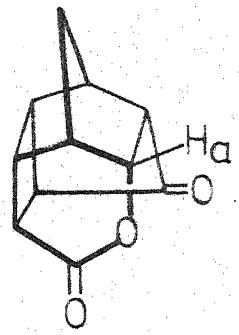


47



48

Oxidation of pentacyclic diketone (22) with CAN in aq. acetonitrile yielded a single crystalline monolactone(45), mp 280-2°, and its structure was derived from the following spectral characteristics. The δ-lactone (45) exhibited intense carbonyl bands at 1780 & 1725 cm^{-1} and displayed in its pmr spectrum a one-proton triplet at δ5.17 (J= 7.5 Hz) due to H-C(-)-O-C(=O)- type grouping (Fig. IV.6). The mass spectral (M^+ 190) fragmentation with strong peaks at m/e 146 ($M^+ - CO_2$), 145 ($M^+ - CO_2H$), 118 ($M^+ - CO_2 - CO$) and 117 ($M^+ - CO_2 - CO - H$) was in complete harmony with a ketolactone structure. The hypsochromic shift of the δ-lactone carbonyl (1780 cm^{-1}) and the bathochromic shift of the cyclopentanone carbonyl (1725 cm^{-1}) in the ir spectrum of 45 can be attributed to the contribution of the form 47. In the alternative structure 46 for this



45

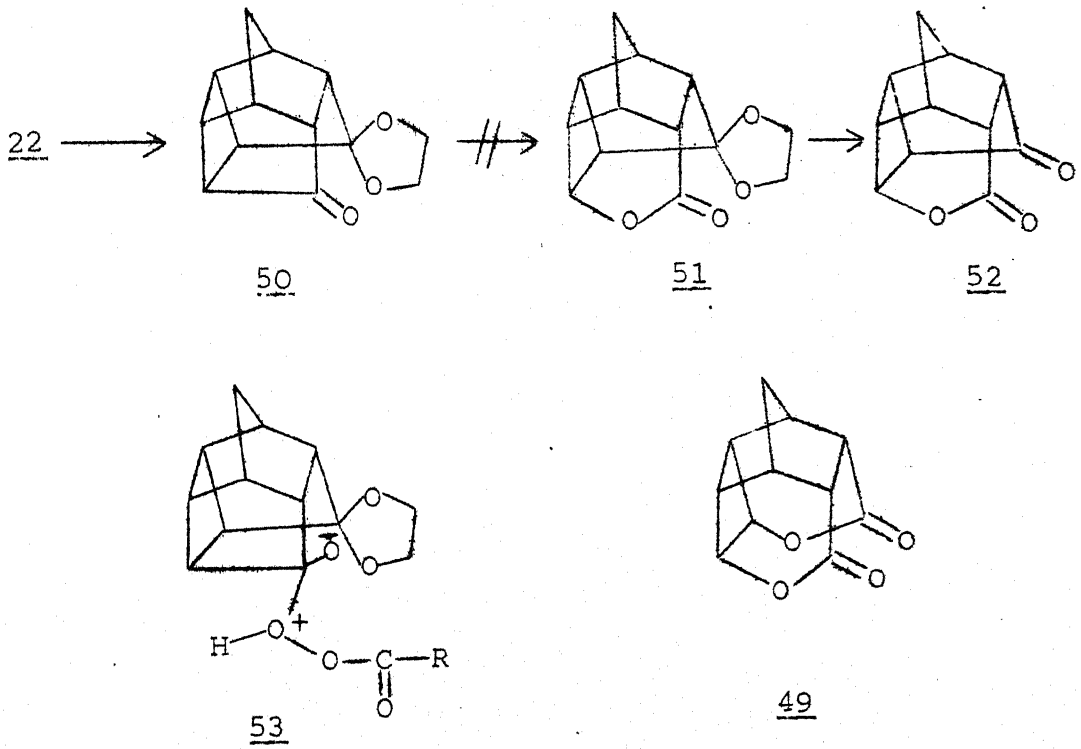
Fig. IV.6 PMR spectrum (60MHz) of 45

lactone such a spatial interaction 48 is precluded on account of unfavourable geometry.

Reaction of 22 with m-chloroperbenzoic acid under a variety of conditions led to the isolation of only a dilactone (49), mp>300°, ir: 1760 cm^{-1} (δ-lactone), MS: M^+ 207? and no monolactonic product could be detected. Due to insolubility of this dilactone (49) in most of the common pmr solvents a satisfactory pmr spectrum for it could not be obtained. However, in analogy with the 1,3-bishomocubanone (20) oxidation, this dilactone is tentatively assigned structure 49. It appears that the presence of a second carbonyl group in 22 complicates its peracid oxidation and in this case the preparative utility of ceric ion in effecting BV oxidation is clearly demonstrated.

In order to prepare a monolactone from 22 via peracid oxidation, another synthetic route (Scheme IV.18) was also explored. Monoketalisation of diketone (22) with ethylene glycol in presence of p-toluenesulphonic acid furnished a crystalline ketone-ketal (50), mp 78°, M^+ 218, ir: 1095, 1045 cm^{-1} (ketal bands), pmr: δ 3.85 ($-CH_2-O-\dot{C}H_2$, 4H, br, s). This monoketal (50) was found to be completely inert towards peracid oxidation under a variety of conditions. It seems likely that steric congestion inside the polycyclic cavity, due to the presence of spiroketal function, prevents the nucleophilic addition 53 of peracid on the carbonyl group.

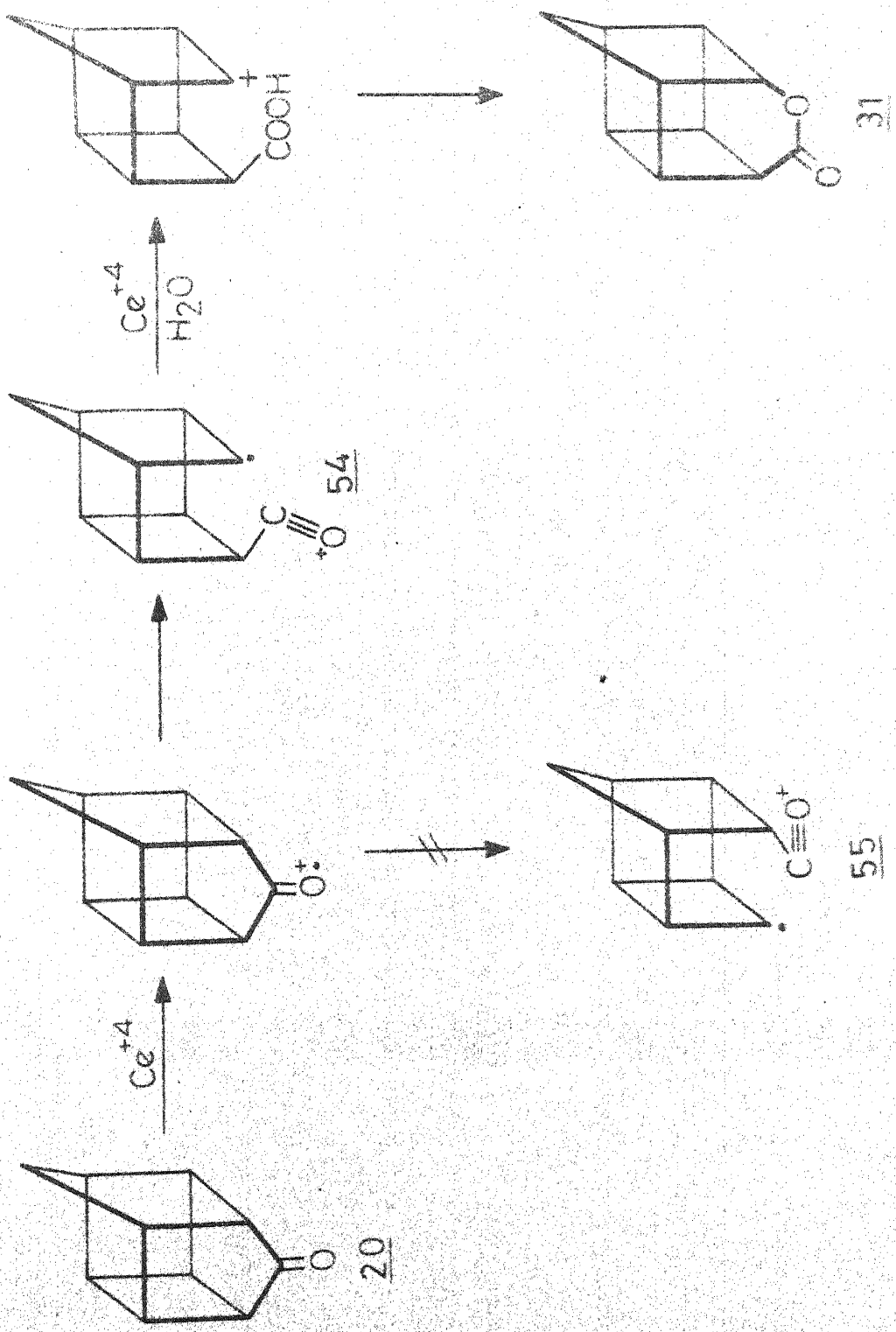
Scheme IV.18



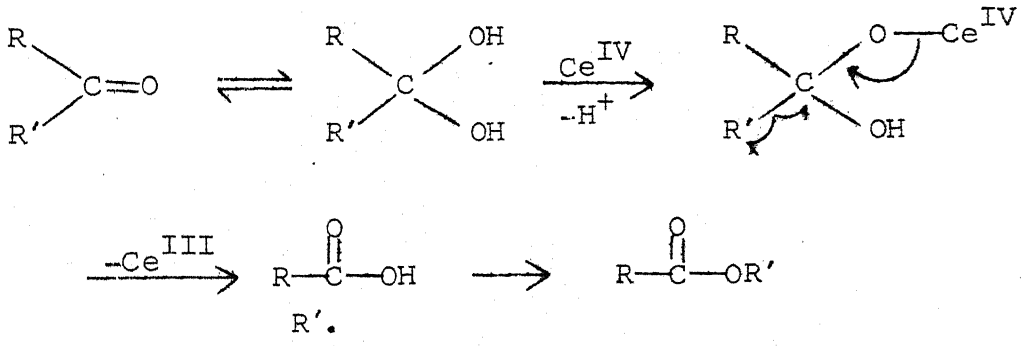
A plausible mechanism for the formation of lactone (31) in the CAS oxidation of 20 is outlined in Scheme IV.19 and is in harmony with the currently accepted mechanism[13] of ceric ion oxidations. There exists an alternate possibility that the ceric oxidation might preferably occur via the hydrates of the ketones as shown in Scheme IV.20. However, this possibility is discounted as we did not observe the deep red colour of the solution upon mixing the oxidant with the substrate which is characteristic[4] of ceric oxidation of alcohols.

The regiospecificity of this reaction can be attributed to the greater stability of cyclopentyl radical intermediate 54 over the cyclobutyl radical intermediate 55. It has not been

Scheme IV 16



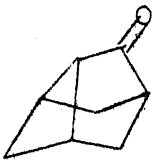
Scheme IV.20



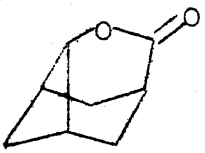
ppssible to locate experimental data in the literature to support this supposition but one can empirically analyse the situation in the following manner. The extracyclic bonds of cyclobutane have more S-character than those of cyclopentane. Thus, assuming that the free radicals have planar structure, they are more difficultly accommodated at a cyclobutane than at a cyclopentane carbon. This selective α-cleavage to furnish the more stable radical intermediate should be useful in the regiospecific BV oxidation of polycyclic ketones and the efficient 22 ⟶ 45 oxidation with ceric ion further strengthens this contention.

On the other hand, regioselective formation of lactone (32) in the peracid oxidation of 20 clearly indicated preferential migration of cyclobutyl ring vs the cyclopentyl ring. Recently, Monti and Ward[44] observed in the BV oxidation of tricyclo[3.2.1.$0^{3,6}$]octan-7-one (56) that the cyclobutyl migration was overwhelmingly favoured and lactone (57) was exclusively formed. Such preferential migration of cyclobutyl

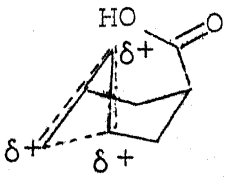
ring was not observed in simple model systems (Scheme IV.21) and therefore regiospecific formation of lactone (57) was attributed to the σ-assisted C-C bond cleavage and stabilisation



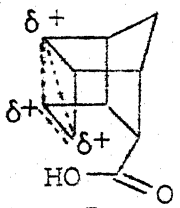
56



57



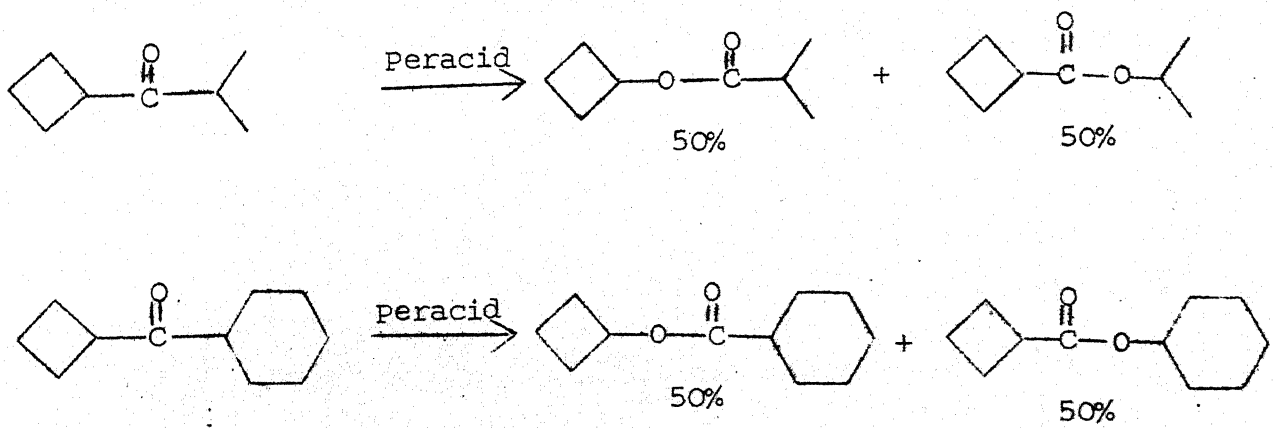
58



59

of the incipient positive charge through a cyclobutyl-cyclopropyl-carbinyl type resonance 58. The results obtained with 20 are likewise suggestive of σ-participation by the strained

Scheme IV.21



C_3-C_4 cyclobutyl bond and stabilisation of the developing positive charge via a cyclobutyl-cyclopropyl-carbinyl type resonance 59. The rigid framework of 20 and favourable geometrical disposition of C_3-C_4 bond makes this participation possible and is fully borne out by an examination of molecular models.

IV.4 EXPERIMENTAL SECTION

Melting points and boiling points are uncorrected. Melting points were taken in capillaries on a Thomas-Hoover melting point apparatus. Boiling points refer to bath temperature in those cases where short path bulb to bulb distillations were carried out. The petroleum ether corresponds to fraction 60-80°. All solvent extracts were dried over anhydrous sodium sulphate. Infrared spectra were recorded on a Perkin-Elmer Model 137B Spectrophotometer as neat liquids or solids as KBr discs. Pmr spectra were obtained an approximately 10-15% solutions in CCl_4 or $CDCl_3$ on a Varian A-60 spectrometer. The chemical shifts are reported in part per million down field from internal tetramethylsilane at 0.00 as internal standard. The abbreviations s, d, t, q, m and en refer to singlet, doublet, triplet, quartet, multiplet and envelop respectively. Microanalysis were performed by Mr. A.H. Siddiqui in the microanalytical laboratory of our department.

Tricyclo[5.2.1.$o^{2,6}$]deca-4,8-dien-3-ol (α-1-hydroxydicyclopentadiene 24)[45]

α-1-Hydroxydicyclopentadiene (24) was prepared from endo-dicyclopentadiene (23) according to the procedure of Woodward and Katz.[45] Thus, a mixture of freshly distilled dicyclopentadiene (23, 40 g, 0.3 mol), dioxane (110 ml), water (12 ml) and disodium hydrogen phosphate (4.5 g) was heated up to 90-95° with stirring in an oil-bath and selenium dioxide (18 g, 0.16 mol) was slowly added. After 5 hr, the reaction mixture was cooled and the precipitated selenium was filtered and washed with ether (50 ml). The filtrate was diluted with 100 ml of brine and thoroughly extracted with ether (150 ml x 3). The organic phase was washed with 5% NaOH solution (50 ml x 2) and with brine. Drying and removal of solvent yielded 34 g of crude oil, which on distillation gave 28 g (64%) of α-1-hydroxydicyclopentadiene (24), bp 85°/3 mm (lit.[45] 67°/0.1 mm).

IR spectrum (neat): 3450, 1020 (hydroxyl) and 3075 cm^{-1} (olefinic).

Tricyclo[5.2.1.$o^{2,6}$]deca-4,8-dien-3-one (endo-dicyclopentadienone 25)

A solution of α-1-hydroxydicyclopentadiene (24, 32 g, 0.208 mol) in acetone (400 ml) was cooled in an ice-bath and titrated with a total of 135 ml of Jones reagent prepared according to the standard procedure. The reaction mixture was stirred at room temperature for 2 hr and then poured into

500 ml of brine and extracted with ether (150 ml x 3). The combined ether extracts were washed and dried. Evaporation of solvent left an oily residue which solidified on standing. Recrystallisation from pet ether gave 25 as a white solid 23.5 g (74%), mp 78-79° (lit.[46] 80°).

IR spectrum (KBr): 1715 cm^{-1} (carbonyl).

PMR spectrum (CCl_4): δ 7.53 (H-C=CH-C=O, 1H, q, J_1= 5 Hz, J2= 3 Hz), 6.0 (rest of the olefinic protons, 3H, m), 3.7-1.5 (C-H ring, 6H, en).

Pentacyclo[5.3.0.$0^{2,5}$.$0^{3,9}$.$0^{4,8}$]decan-6-one (1,3-Bishomocubanone, 20)[35]

A solution of endo-dicyclopentadienone (25, 10 g) in dry cyclohexane (1 l) was purged with a slow stream of purified nitrogen for 30 min. This solution was irradiated in a quartz immersion well with a 450W Hanovia medium pressure mercury arc lamp for 20 hr till all the starting ketone was consumed (tlc). The turbid reaction product containing some suspended polymeric impurities was filtered and the solvent was removed under vacuum to yield 11.5 g of crude product. Filtration of the crude product through a silica gel column (150 g) using 50% benzene-pet ether and direct sublimation (70-80°/10 mm) yielded 6.8 g (68%) of 1,3-bishomocubanone (20) as a white solid, mp 122-24° (lit.[35] 122-126°).

IR spectrum (KBr): 1750 cm^{-1} (carbonyl).

PMR spectrum ($CDCl_3$): δ 2.23 and 2.42 (-C<u>H</u>-C(=O)-C-<u>H</u>, 2H, br, s), 1.68 ($\underline{H_2}C$-, 2H, q, J= 12 Hz), 2.7-3.32 (C-H ring, 6H, en).

anti-Pentacyclo[5.3.0.$0^{2,5}$.$0^{3,9}$.$0^{4,8}$]decan-6-ol (26)[47]

A solution of α-1-hydroxydicyclopentadiene (24, 10 g, 0.068 mol) in acetone (150 ml) was degassed by a stream of purified nitrogen for 20 min. The solution was then irradiated under a nitrogen blanket employing a 450W Hanovia medium pressure mercury arc lamp in a quartz immersion well using a vycore 512 filter for 7 hr. The solvent was removed under reduced pressure to give 13 g of a yellowish viscous oil. Direct sublimation (120°/3 mm) yielded 5.9 g of a soft white solid. Recrystallisation from pet ether furnished 3.4 g (34%) of 26 as white needles, mp 166-67° (lit.164-66,[47] 171-72°[35]).

IR spectrum (KBr): 3350, 1070 and 1040 cm^{-1} (hydroxyl).

PMR spectrum (CCl_4): δ 4.28 (-C<u>H</u>-OH, 1H, s), 1.62 and 1.20 ($-CH_2-$, 2H, pair of d, J_{gem}= 11 Hz), 3.0-2.25 (C-H ring, 7H, en).

Preparation of pentacyclo[5.3.0.$0^{2,6}$.$0^{3,9}$.$0^{4,8}$]decan-5-one (1,4-Bishomocubanone, 21)[36]

anti-1,3-Bishomocubanol (26, 1.4 g, 9 mmol) and p-toluenesulphonyl chloride (2 g, 9.9 mmol) in pyridine (10 ml) were mixed at 0° and stirred for 1 hr. The reaction mixture was

further stirred at room temperature for 2 hr and then poured into ice-water (50 ml) and extracted with methylene chloride (25 ml x 3). Combined organic phase was washed twice with 10% HCl (50 ml) and with brine. Drying and removal of solvent gave 2.8 g of crude tosylate. Recrystallisation from pet ether furnished 2.6 g (88%) of 1,3-bishomocubyl tosylate (27) as white solid, mp 87-88° (lit.[36] 88-88.5°).

IR spectrum (KBr): 1360 and 1180 cm^{-1} (tosylate).

A solution of the above tosylate (27, 2.4 g, 7.8 mmol) in glacial acetic acid (150 ml) was heated at 120° for 42 hr. The reaction mixture was poured into 500 ml of water and extracted with methylene chloride (50 ml x 3). The combined organic extracts were successively washed with sodium bicarbonate solution and brine. Drying and removal of solvent gave 1.40 g (90%) of crude acetate (28).

IR spectrum (neat): 1745 and 1240 cm^{-1} (ester).

The above crude acetate (28, 1.2 g, 6.3 mmol) in 10 ml of dry ether was added dropwise to a stirred slurry of lithium aluminium hydride (0.35 g, 9 mmol) in 20 ml of dry ether. After stirring at room temperature for 15 hr the reaction mixture was hydrolysed by careful addition of 5% sodium hydroxide solution (2 ml). The reaction mixture was diluted with water and filtered to remove precipitated salts. The filtrate was extracted with ether (15 ml x 2), washed and dried. Removal of solvent yielded 0.85 g (92%) of crude

1,4-bishomocubanol (29). Purification was achieved via two recrystallisations from pet ether, mp 139-40° (lit. 143-44°,[36] 137-140°[48]).

IR spectrum (KBr): 3340, 1075 cm^{-1} (hydroxyl).

To an ice-cooled solution of 1,4-bishomocubanol (29, 0.8 g, 5.4 mmol) in acetone (20 ml) was added Jones reagent (4 ml) dropwise till yellow colour persisted. The reaction mixture was stirred at ambient temperature for 2 hr and then poured into water (15 ml). Extraction with ether (20 ml x 3), washing, drying and removal of solvent gave 1,4-bishomocubanone (21), 0.6 g (75%). Recrystallisation from pet ether furnished white crystals, mp 122-23° (lit, 119-22°[36], 123°[49]).

IR spectrum (KBr): 1750 cm^{-1} (carbonyl).

PMR spectrum (CCl_4): δ 1.44 ($\underline{H}_2C$-, 2H, t, J= 3 Hz), 3.6-2.55 (C-H ring, 8H, en).

Cyclopentadiene-p-benzoquinone adduct (30)[50]

To an ice-cold solution of freshly crystallised p-benzoquinone (20 g, 0.18 mol) in dry benzene (50 ml) was added freshly distilled cyclopentadiene (12.3 g, 0.18 mol) with gentle swirling of the flask. After the addition was complete, the reaction flask was left aside at room temperature for 2 hr for crystallization. Filtration gave the adduct (30), 28 g (88%) as pale crystals, mp 76° (lit.[50] 75-76°).

IR spectrum (KBr): 1670 (carbonyl), 835 and 750 cm^{-1}.

PMR spectrum ($CDCl_3$): δ6.4 (O=C-CH=CH-C=O, 2H, s), 5.94 (H-C=C-H, 2H, s), 3.4 and 3.12 (C-H ring, 4H, pair of s), 1.4 ($-CH_2$, 2H, s).

Pentacyclo[6.2.1.$0^{2,7}$.$0^{4,10}$.$0^{5,9}$]undecan-3,6-dione (22)[37]

A solution of the adduct (30, 15 g) in ethyl acetate (200 ml) was purged with a slow stream of purified nitrogen for 25 min. The solution was then irradiated with a 450W Hanovia medium pressure mercury arc lamp for 7 hr in a pyrex immersion well. Removal of the solvent and direct crystallisation from benzene-pet ether mixture furnished white stout crystals of diketone (22), 13 g (87%), mp 243-44° (lit.[37] 245°).

IR spectrum (KBr): 1750 cm^{-1} (carbonyl).

PMR spectrum ($CDCl_3$): δ 1.7 ($-CH_2$, 2H, q), 3.0-2.2 (C-H ring, 8H, en).

Oxidation of pentacyclo[5.3.0.$0^{2,5}$.$0^{3,9}$.$0^{4,8}$]decan-6-one (20) with Ceric ammonium sulphate

To a magnetically stirred slurry of ceric ammonium sulphate (18 g, 28 mmol) in water (35 ml) in a 100 ml RB flask, a solution of bishomocubanone (20, 1 g, 6.9 mmol) in acetonitrile (18 ml) was added. The reaction mixture was heated at 60° for 1 hr and cooled to room temperature. Dilution with water, extraction with methylene chloride (25 ml x 2), washing, drying and evaporation of solvent gave 1.05 g of a waxy solid. Elution of

this material from a silica-gel (30 g) column with benzene yielded 0.86 g (78%) of pure lactone (31), which on sublimation (80° at 1 mm) gave white glistening solid, mp 133-5°.

IR spectrum (KBr): 1760, 1180, 1000 cm^{-1} (lactone).

PMR spectrum (CCl_4): δ 5.05 (H-C(-O-C(=O)-), 1H, q , J_1= 4 Hz, J_2 = 3 Hz), 1.25-3.2 (C-H ring, 9H, en).

MS (m/e): 162(M^+), 118 (M^+-CO_2), 117 (M^+-CO_2H), 105,103, 91 ($C_7H_7^+$), 84, 79, 66 ($C_5H_6^+$).

Anal. for $C_{10}OH_{10}O_2$: Calcd; C, 74.05; H, 6.22.
Found: C, 74.30; H, 6.00.

Oxidation of 1,3-bishomocubanone (20) with m-chloroperbenzoic acid

To a solution of (20, 0.1 g, 0.7 mmol) in dry benzene (10 ml), m-chloroperbenzoic acid (0.15 g, 0.87 mmol, Aldrich) and catalytic amount of p-toluene sulphonic acid (50 mg) were added with gentle swirling of the flask. Reaction was completed in two hr (tlc) and the mixture was poured into water (10 ml), extracted with ether (20 ml x 2) and washed with aq. sodium bicarbonate (10 ml x 3). Removal of solvent yielded a waxy solid 0.10 g (90%), which was found to be a mixture of lactones (32) and (31) in a ratio of 5:1 (pmr integration). Separation of the two lactones was achieved by preparative tlc on silica gel plates (20 x 20 cm) using benzene-ethyl acetate (4:1) as the solvent system. The fast moving minor

component was identical with the lactone (31) formed in the CAS oxidation of 20. The major component was sublimed (80°/ 1 mm) to yield 0.05 g of white crystals, mp 145-46°.

IR spectrum (KBr): 1755, 1365, 1070 cm^{-1} (lactone).

PMR spectrum (CCl_4): δ 4.7 (H-C(-)-O-C(=O)-, 1H, t, J= 6 Hz), 1.6-3.4 (C-H ring, 9H, en).

MS (m/e): 162 (M^+), 118 ($M-CO_2$), 117 (M^+-CO_2-H), 91 ($C_7H_7^+$), 66 ($C_5H_6^+$).

Anal. for $C_{10}H_{10}O_2$: Calcd; C, 74.05; H, 6.22.
Found; C, 74.36; H, 6.30.

LAH reduction of lactone (31)

Lactone (31, 0.7 g, 4.3 mmol) in dry ether (25 ml) was added slowly to a slurry of lithium aluminium hydride (0.3 g, 7.9 mmol) in dry ether (15 ml). The reaction mixture was stirred for 12 hr at room temperature and then quenched by adding slowly 3 ml of water and 1 ml of 15% potassium hydroxide. Extraction with methylene chloride (20 ml x 2) yielded 0.6 g of crude diol. Crystallisation from ether gave glistening white needle 0.5 g (70%) of 33, mp 125°.

IR spectrum (KBr): 3450 (hydroxyl), 1000, 1075 cm^{-1}.

PMR spectrum ($CDCl_3$) δ 4.5 (H-C(-)-OH, 1H, m), 4.03 (H_2C-OH, 2H, m), 1.2-2.65 (C-H ring and -OH, 11H, en).

MS (m/e): 148 (M^+-H_2O), 117, 120 ($C_9H_{12}^+$), 91 ($C_7H_7^+$), 79 ($C_5H_3O^+$ or $C_6H_7^+$), 66 ($C_5H_6^+$).

Anal. for $C_{10}H_{14}O_2$: Calcd C, 72.26; H, 8.49.
Found C, 72.21; H, 8.35.

Acid catalysed cyclisation of diol (33) to pentacyclic ether(36)

The above diol (33, 0.1 g, 0.6 mmol) in dry benzene (10 ml) containing p-toluene sulphonic acid (10 mg) was refluxed for 2 hr. The reaction mixture was poured into sodium carbonate solution (10 ml, 5%) and extracted with ether (20 ml x 2). Washing, drying and removal of solvent gave a waxy residue showing single spot on tlc. Sublimation (60° at 1 mm) of this material yielded 0.08 g (90%) of 36 as a white crystalline solid, mp 140°.

IR spectrum (KBr): 1025 cm^{-1} (ether).

PMR spectrum (CCl_4): δ4.8 (H-C-O-, 1H, m). 4.0 ($-CH_2-O-$, 2H, m), 1.2-2.75 (C-H ring, 9H, en).

MS (m/e): 148 (M^+), 120 (M^+-CO), 117, 91 $(C_7H_7)^+$, 79 ($C_5H_3O^+$ or $C_6H_7^+$), 69 ($C_4H_5O^+$).

Anal. for $C_{10}H_{12}O$: Calcd C, 81.04; H, 8.16.
Found C, 80.89; H, 8.09.

Jones oxidation of diol (33)

An ice cooled stirred solution of the diol (33, 0.2 g, 1.2 mmol) in 5 ml of acetone was treated dropwise with Jones reagent (2 ml)until the yellow colour persisted. The mixture was stirred for 4 hr, diluted with water, and extracted with ether

(25 ml x 2). The organic layer was successively washed with sodium carbonate, brine and dried. Removal of solvent gave 0.04 g of product, which was identified as lactone (31). Water layer was acidified with 15% HCl and extracted with methylene chloride (25 ml x 3) to give 0.13 g of keto acid (34).

IR spectrum (KBr): 3375, 1740, 1725, 1245 cm^{-1}.

Keto ester (35)

To a solution of the above keto acid (34, 0.1 g) in dry ether, an ethereal solution of diazomethane was added till permanent yellow colour persisted. The reaction mixture was left aside for 1 hr and excess of diazomethane was neutralised by careful addition of acetic acid. Removal of solvent and direct distillation gave keto ester (35) as a colourless liquid, bp 110-15° (bath, 1 mm).

IR spectrum (neat): 1740, 1730, 1180 cm^{-1}.

PMR spectrum (CCl_4): δ 3.67 ($\underline{CH_3}$-O-$\overset{O}{\overset{\|}{C}}$-, 3H, s), 1.5-3.1 (C-$\underline{H}$ ring, 9H, en).

MS (m/e): 192 (M^+), 164 (M^+-CO), 161 (M^+-OCH_3), 131 (M^+-CO_2Me), 114, 79 ($C_5H_3O^+$ or $C_6H_7^+$).

Anal. for $C_{11}H_{12}O_3$: Calcd C, 68.73; H, 6.29.
Found C, 68.53; H, 6.14.

LAH reduction of lactone (32)

Lactone (32, 0.7 g, 4.3 mmol) in dry ether (25 ml) was added slowly to a slurry of lithium aluminium hydride (0.3 g, 7.9 mmol) in dry ether (15 ml). The reaction mixture was stirred for 8 hr at room temperature. Work-up as described earlier and extraction with methylene chloride (25 ml x 2), drying and removal of solvent gave 0.65 g of a waxy product. Elution of this material from silica gel column with benzene yielded 0.3 g (45%) of ether (37). On sublimation (140° at 1 mm) it gave white crystalline solid, mp 192°.

IR spectrum (KBr): 1025, 995 cm^{-1}.

PMR spectrum (CCl_4): δ5.52 ($\underline{H}$-C(-O-)-, 1H, m), 4.13 ($\underline{H_2}$-C(-O-)-, 2H, t, J= 5 Hz), 1.3-3.3 (C-$\underline{H}$ ring, 9H, en).

MS (m/e): 148 (M^+), 117, 91 ($C_7H_7^+$), 81 ($C_5H_5O^+$), 79 ($C_5H_3O^+$ or $C_6H_7^+$).

Anal. for $C_{10}H_{12}O$: Calcd C, 81.04; H, 8.16.
Found C, 80.94; H, 7.95.

Addition of methyl magnesium iodide to lactone (32)

Methyl magnesium iodide (from 0.1 g of magnesium turnings and methyl iodide (0.6 g) in 25 ml dry ether) was prepared according to usual procedure and lactone (32, 0.25 g, 1.5 mmol) in 5 ml of dry ether was dropwise added with continuous stirring. The reaction mixture was quenched after 3 hr with 10% ammonium chloride (5 ml) and extracted with ether

(25 ml x 2). Washing drying and evaporation of solvent yielded 0.3 g of crude lactol (40), which was crystallised from benzene pet ether (1:4) to furnish white stout crystals 0.2 g (72%), mp 114-15°.

IR spectrum (KBr): 3550 (hydroxyl), 1055, 920 (ether) cm^{-1}.

PMR spectrum (CCl_4): δ 4.05 (-$\overset{H}{\underset{|}{C}}$-O-, 1H, 5 Hz), 1.38($H_3C$-$\overset{|}{\underset{|}{C}}$-OH, 3H, s), 1.8-3.2 (C-H ring and O-H, 1OH, en).

Anal. for $C_{11}H_{14}O_2$: Calcd; C, 74.13; H, 7.92.
Found; C, 74.39; H, 8.17.

Jones oxidation of lactol (40)

To an ice-cold solution of lactol (40, 0.1 g, 0.56 mmol) in acetone (5 ml) was added Jones reagent (0.5 ml) dropwise till yellow colour persisted. The reaction mixture was stirred overnight at room temperature and then poured into water (10 ml), Extracted with ether (20 ml x 2), washed with 10% sodium carbonate solution (10 ml x 2), brine and removal of solvent gave diketone (41), 0.075 g (75%).

IR spectrum (neat): 1775 (cyclobutanone), 1720 cm^{-1}.

Addition of methyl magnesium iodide to lactone (31)

Methyl magnesium iodide (from (0.15 g) of magnesium turnings and methyl iodide (0.9 g) in 25 ml dry ether) was prepared according to usual procedure and lactone(31, 0.4 g, 2.25 mmol) in 10 ml of dry ether was dropwise added with continuous stirring. The reaction mixture was quenched after 2 hr

with 10% ammonium chloride (10 ml) and extracted with ether (25 ml x 2). Washing, drying and removal of solvent, yielded 0.48 g of crude lactol (42). Filtration from silica gel column using 1:4 ethylacetate-benzene as a solvent and crystallisation from pet ether-benzene mixture furnished white flakes 0.31 g (70%), mp 89-90°.

IR spectrum (KBr): 3500 (hydroxyl), 1010, 1050 (ether) cm^{-1}.

PMR spectrum (CCl_4): δ 4.8 (H-C-O-, 1H, m), 1.6 (CH_3-C-OH, 3H, s), 1.3-3.95 (C-H ring and O-H, 10H, en).

Anal. for $C_{11}H_{14}O_2$: Calcd C, 74.13; H, 7.92.
Found C, 74.41; H, 7.79.

Jones oxidation of lactol (42)

To an ice-cold solution of lactol (42, 0.25 g, 1.4 mmol) in acetone (10 ml) was added Jones reagent (1 ml) dropwise till yellow colour persisted. The reaction mixture was stirred overnight at room temperature and then poured into water(15 ml). Extraction with ether(20 ml x 2),washing with 10% sodium carbonate solution, brine and removal of solvent yielded diketone (43), 0.18 g (70%).

IR spectrum (neat): 1740 (cyclopentanone), 1718 cm^{-1}.

Oxidation of pentacyclo[5.3.0.$0^{2,6}$.$0^{3,9}$.$0^{4,8}$]decan-5-one (21) with ceric ammonium sulphate

To a magnetically stirred slurry of ceric ammonium sulphate (3.5 g, 5.5 mmol) in water (7 ml) a solution of

1,4-bishomocubanone (21, 0.2 g, 1.4 mmol) in acetonitrile (3.5 ml) was added. Reaction mixture was stirred at 60° for 3 hr and worked up as described earlier to yield 0.2 g of a waxy solid. Direct sublimation (75° at 1 mm) gave 0.175 g (80%) white crystals of 44, mp 130-32°.

IR spectrum (KBr): 1755, 1260, 1075 cm^{-1} (lactone).

PMR spectrum (CCl_4): δ 5.0 (H-C(-O-C(=O))-, 1H, m), 1.5-3.5 (C-H ring, 10H, en).

Anal. for $C_{10}H_{10}O_2$: Calcd C, 74.08; H, 6.17.
Found C, 74.13; H, 6.15.

Oxidation of (21) with m-chloroperbenzoic acid

To a solution of 1,4-bishomocubanone (21, 0.1 g, 0.7 mmol) in dry benzene (10 ml) was added m-chloroperbenzoic acid (0.15 g, 0.87 mmol, Aldrich) and catalytic amount of p-toluene sulphonic acid with gentle swirling of the flask. Reaction was complete in 2 hr (tlc) and usual work-up as described in earlier case yielded 0.095 g (85%) of lactone (44) identical with the CAS oxidation product of (21).

Oxidation of pentacyclo[6.2.1.$0^{2,7}$.$0^{4,10}$.$0^{5,9}$]undecan-3,6-dione (22) with ceric ammonium nitrate

To a magnetically stirred slurry of ceric ammonium nitrate (16 g, 30 mmol) in water (30 ml) a solution of diketone (22, 1 g, 5.7 mmol) in acetonitrile (20 ml) was added. Reaction mixture was stirred at 30° for 1 hr and

worked up as described above to yield 1.1 g of a solid residue. Direct recrystallisation from methylene chloride- ether gave 0.9 g (82%) colourless crystals of 45, mp 280-2°.

IR spectrum (CH_2Cl_2): 1780 (δ -lactone), 1725 cm^{-1} (cyclopentanone).

PMR spectrum ($CDCl_3$): δ 5.17 (H-C(-O)-O-C(=O)-, 1H, t, J= 7.5 Hz), 2.45-3.4 (C-H ring, 5H, en), 1.7-2.3 (C-H ring, 4H, m).

MS (m/e): 190 (M^+), 146 ($M^+ - CO_2$), 145 ($M^+ CO_2H$), 118 ($M^+ CO_2$-CO), 117 (M^+-CO_2-CO-H), 91 ($C_7H_7^+$), 79 ($C_5H_3O^+$ or $C_6H_7^+$), 66 ($C_5H_6^+$).

Anal. for $C_{11}H_{10}O_3$: Calcd C, 69.46; H, 5.30.
Found C, 69.63; H, 5.19.

Oxidation of (22) with m-chloroperbenzoic acid

To a solution of diketone (22, 0.25 g, 1.4 mmol) in dry benzene (15 ml) was added m-chloroperbenzoic acid (0.29 g, 1.4 mmol, Aldrich) and catalytic amount of p-toluene sulphonic acid with gentle swirling of the flask. Reaction was complete in 2 hr and usual work-up as described in case of 20 yielded 0.28 g of dilactone (49). Recrystallisation from methylene chloride gave colourless micro needles (0.13 g, 45%), mp>300°.

IR spectrum (CH_2Cl_2): 1760 cm^{-1} (δ -lactone).

MS (m/e): 207? (M^+ + 1), 206 (M^+), 178 (M^+-CO), 150 (M^+ -2 CO), 134 (M^+-CO_2-CO).

The pmr spectrum of 49 could not be recorded due to its insolubility in $CDCl_3$ and $(CD_3)_2C=O$.

Anal. for $C_{11}H_{10}O_4$: Calcd C, 64.07; H, 4.89.
Found C, 63.86; H, 4.73.

The mother liquor from the recrystallisation of 49 showed the presence of unreacted starting material. When BV oxidation of diketone (22) (0.25 g, 1.4 mmol) was carried out with m-chloroperbenzoic acid (0.58 g, 2.8 mmol) as described above, dilactone(49) was obtained in 90% yield.

Monoketal of diketone (22)

In a 250 ml RB flask fitted with a Dean-Stark apparatus, diketone (22, 0.5 g, 2.3 mmol) in dry benzene (100 ml) containing ethylene glycol (2.5 ml) and p-toluenesulphonic acid(50 mg) was refluxed for 7 hr. The mixture was cooled and poured into water (25 ml) and extracted with ether (25 ml x 3). Washing with 10% sodium bicarbonate solution (10 ml x 2), drying and removal of solvent yielded 0.65 g of crude product. Recrystallisation from pet ether furnished 0.55 g (85%) of shining white crystals of keto-ketal (50), mp 78°.

IR spectrum (KBr): 1760(carbonyl), 1345, 1095, 1045 and 1010 cm^{-1} (ketal).

PMR spectrum (CCl_4): δ 3.85 ($-\underline{CH_2}-O-\underline{CH_2}-$, 4H, br, s), 1.68 ($-CH_2-$, 2H, q), 2.9-2.2 (C-H ring, 8H, en).

MS (m/e): 218 (M^+), 190 ($M^+-C_2H_4$), 152 ($M^+-C_5H_6$), 117, 99, 91 ($C_7H_7^+$), 73, 66 ($C_5H_6^+$).

Anal. for $C_{13}H_{14}O_3$: Calcd C, 71.54; H, 6.47.
Found C, 71.69; H, 6.38.

Oxidation of keto-ketal (50) with m-chloroperbenzoic acid

To a solution of keto-ketal (50, 0.25 g, 1.2 mmol), in dry benzene (10 ml), m-chloroperbenzoic acid (0.24 g, 1.2 mmol, Aldrich), and catalytic amount of p-toluenesulphonic acid were added with gentle swirling of the flask. The reaction mixture was left aside at room temp for several days. Careful monitoring by tlc indicated that starting material is not being consumed. This was further confirmed by recovering back the starting material after usual work-up.

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LIST OF PUBLICATIONS

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